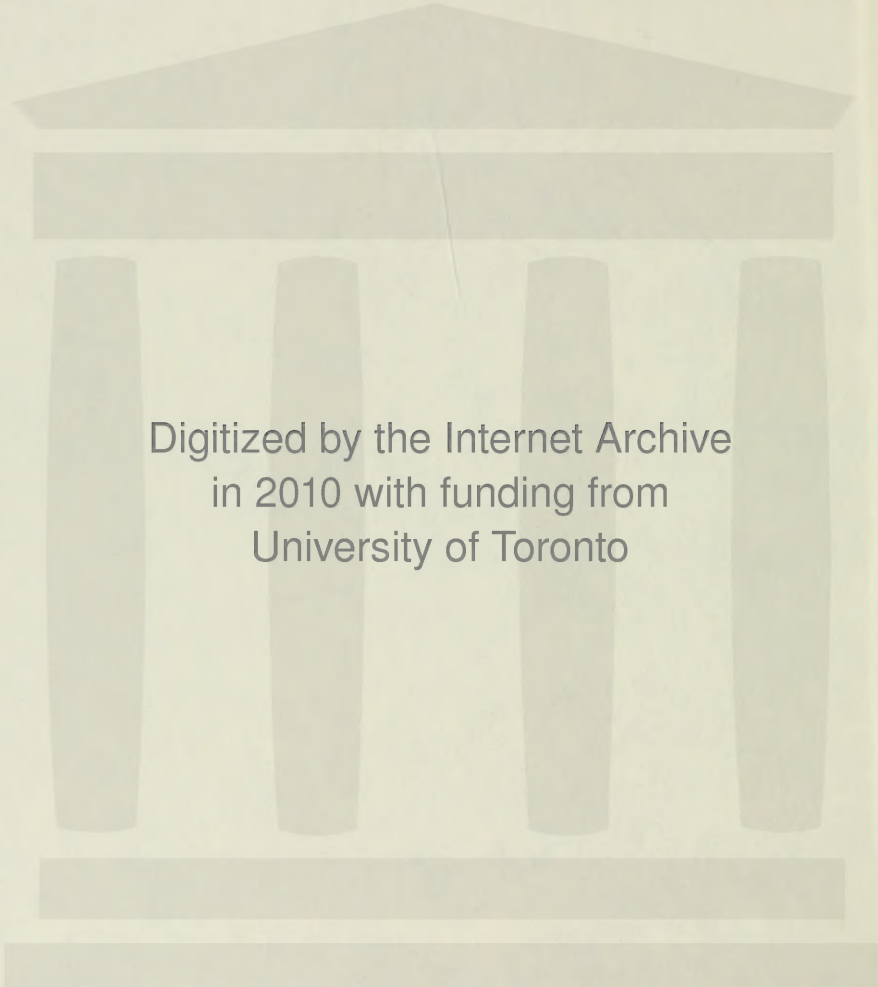
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SOME CHARACTERISTICS OF THE MEDICINE IN SHAKESPEARE

By Arthur W. Meyer,

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But why should I dead Shakespeare's praise recite?
Some second Shakespeare must of Shakespeare write.
—Leonard Digges.

If it be a rule that no one should write about Shakespeare without a license I stand convicted. I have no license and cherish no hope for any. Neither am I a "thorough antiquarian" or "heaven-born critic" as Leslie Stephen prefers. Yet, since the master whom "I serve quickens what's dead," I trust that this delineation, the product of *horæ subsecivæ*, may not prove "as tedious as a twice-told tale vexing the ear of a drowsy man."

To those familiar with the literature on the medicine of Shakespeare, many reasons for further study of this too oft rediscovered subject will come to mind. It is not my purpose, however, to "anatomize" specific medical references or to pass judgment upon the medical knowledge of Shakespeare. Far be it from me. Such a judgment cannot be based upon the plays alone. Shakespeare's knowledge of medicine and his attitude toward physicians may be reflected in his plays, but this seems to be merely incidental. Obviously, if the characters in Shakespeare express medical facts, Shakespeare himself must have possessed a knowledge of these facts. However, it is the world's life rather than his own that the great dramatist reveals to us in his dramas.

The medical writers of the sixteenth century interested themselves more with the medicine of Hippocrates, Galen, and Rhazes than with that of their own day. Hence it is difficult to form a good conception of the medicine of Shakespeare's time. The death of Vesalius, a few months after the birth of Shakespeare, is perhaps one of the greatest of landmarks. Vesalius's enforced expiatory pilgrimage to the Holy Land, in order to escape sentence by the Spanish Inquisition, vividly recalls the temper of the times. Fancy and imagination were unbridled, suffer who might through the accusations of excited and misguided individuals! Galenism was still supreme. Physicians clung to Galen and accused of heresy all who did not accept his teaching. Hospitals were still in the hands of the priesthood but medicine and surgery had passed from their domination. Yet the activity of the priesthood continued. Almost a century later Gideon Harvey exclaimed, "In short *libera nos* from those who practice medicine in *Nomine Domini*." The Royal College of Physicians, of London, was forty-six years old, and a union of Barber Surgeons and Guild Surgeons known as the Company of Barbers and Surgeons had existed since 1540. Physicians held secrets against the rule; surgeons as a rule. The former wrote in Latin, the latter, though learned, in the vernacular and were ostracised and roundly berated for it. Neither "learned nor unlearned" surgeons had statutory powers. They could not give internal remedies, and their bitter disputes with physicians were to last for centuries. They were slowly freeing themselves, however, from the barbers and

were demanding recognition from the physicians who were loath to grant it. The dictum of Galen that a physician need have no knowledge of surgery still remained the gospel of physicians and the bane of surgeons. However, heroic voices were being raised against the abuses in medicine and physicians no longer deemed it a disgrace to visit their patients. The first herbals had just appeared, yet grocers and apothecaries were still in one company. The latter charged exorbitant fees, prescribed on the reported diagnosis of physicians, and even changed the prescriptions of physicians at will. The value of pathological anatomy had been pointed out, but gynecology, and especially obstetrics, had received but little attention. Yet these were days of universal awakening. Great seats of learning had arisen. Naples, Bologna, Padua, Ferrara, Montpelier, and Paris were famous and destined to become historic. Anatomy had, indeed, made great progress. Vesalius, Fallopius, Eustachius, Sylvius, Aurantius, Bauhin, Spigelius, Botal, and Glisson, were its greatest devotees; and da Vinci, Calcar, Dürer, Michael Angelo, Titian, and Raphael, its artist patrons. Dissections of the human body to which surgeons were summoned by a beadle were made annually in London. These dissections taught physicians to believe their own eyes and to cease apologizing for the inaccuracies in Galen with the plea that human beings were formed differently in Galen's day. Back to the Bible for the theologians became back to the cadaver for the anatomists! The great pestilences which periodically swept over England and over all Europe left the country prostrate. Among these whooping-cough and pleurisy had made their advent. It was customary to look to God, to the stars, and to the devil for the causes, but the pall of superstition was lifting. The world was astir. These were, in short, "the spacious times of great Elizabeth."

To read Shakespeare with a purpose is no easy task. Felicity of expression, interest of plot, depth of pathos, and beauty of character hold one in a magic spell, entirely oblivious of one's quest. Whole pages, scenes, and, perchance, acts must be re-read with the purpose freshly in mind. Consequently any list of medical references obtained by a single reading must be incomplete. However, such a list has been supplemented by consultation of different editions and by comparison with the compilations of various authors. An examination of these references in the light of the medicine of the sixteenth century, of the England of Shakespeare and *of the genius of Shakespeare,* ought to reveal to us the leading characteristics of the medicine of Shakespeare. To examine them, as is so often done, in the light of the present day, is a serious error. For, as Leslie Stephen has well said, "It is, of course, an anachronism to transplant our problems to those days." That this anachronism has frequently been committed even a cursory examination of the literature will show. Things have repeatedly been read into the plays of Shakespeare rather than out of them. Many amusing examples might be given illustrating how "hateful error" has shown "to the apt thoughts of men the things that are not," or that there is no "damned error, but some sober brow

Will bless it, and approve it with a text."

The number of medical references found will vary with the edition used and with the *medical* and *historical perspective of the reader.* A liberal interpretation will naturally include many things which are merely matters of knowledge common to all men. Such, for example, are the following:

He that sleeps feels not the toothache.
—*Cymbeline,* V, 4.

We do lance diseases in our bodies.
—*Antony and Cleopatra,* V, 1.

'Tis dangerous to take a cold.
—*Henry IV,* Pt. I, II, 3.

The more one sickens the worse at ease he is.
—*As You Like It,* III, 2.

Many will swoon when they do look on blood.
—*As You Like It,* IV, 3.

. . . . . a gaping wound
Issuing life blood.
—*A Merchant of Venice,* III, 2.

What wound did ever heal but by degrees?
—*Othello,* II, 3.

That rubbing the poor itch . . . . .
Make yourselves scabs.
—*Coriolanus,* I, 1.

To this class of references belong also the change of voice at puberty, the mere mention of fever, nausea, and God's tokens, the loss of appetite in disease, the obstruction of blood by tight garters, vomiting after surfeiting on sweets, and many medical references which were a part of the superstition of the time. Indeed, the fact that medicine and physicians were surrounded by an atmosphere of superstition often makes it difficult to discriminate between the many vulgar beliefs of that day and medical allusions. The unwary student may thus regard as idle superstition lines pregnant with medical lore. The language, too, in which these medical facts are expressed will depend to some extent upon the edition used, and the meaning of some of them remains obscure and disputed even after the most careful comparison and diligent inquiry. Among these may be mentioned the expressions "hollow bones," "sand-blind," "hebenon," "goodyear and eyesel," for which various explanations have been suggested. In other cases the language is clear but the meaning is obscure. This is true of Portia's method of suicide, of the nature of Cardinal Beaufort's delirium, and in a measure of Ferdinand's avowal,

"I warrant you, sir,
The white cold virgin snow upon my heart
Abates the ardor of my liver."
—*Tempest,* IV, 1.

There remains the important and vexed question of authorship. As a basis for these remarks only those plays or parts of a play which are considered truly Shakespearean have been used. However, the final estimate of the medicine of Shakespeare would not be materially affected by ignoring the

question of authenticity or by adopting either a liberal or a narrow interpretation regarding what shall and what shall not be considered a medical allusion.

The number of medical references in the different Shakespearean plays varies considerably. As might be expected comedies as a rule contain fewer than the tragedies and historical plays. In the historical plays, and especially in the tragedies, pestilences and their supposedly mysterious and evil origin, poisons with their strange and sinister powers, and death with its consequent political intrigues and conflicts, its trials and pathos, offer a necessary material. The poems and sonnets contain at most a few dozen references, and the greater number of these are found in the Rape of Lucrece. They embody nothing especially characteristic save that the medicine of some of them, like the surgery in Titus Andronicus, is quite impossible. If we except Henry IV and VI, the later plays contain more medical expressions than the earlier ones. Yet it seems impossible to demonstrate—what must have taken place—a definite growth in Shakespeare's medical horizon. Henry VI, which belongs in the first years of Shakespeare's literary activity, contains more numerous medical references than any other play. This, however, is largely accounted for by its being composed of three parts, thus making a much longer play. The same is true of Henry IV. However, the important thing is not the actual number of references in any one play, but rather the total number which are found in Shakespeare's earlier, as compared with his later, works. Among other plays containing many medical references are King John, Coriolanus, Othello, Troilus and Cressida, the Winter's Tale, and Hamlet. Plays in which a physisian enters contain no more medical references. Strange as it may seem at first sight, the physicians are minor characters who contribute little or nothing to the fund of medical knowledge. The words which they utter could usually be spoken by anyone in their stead. Their presence is, as a rule, demanded by the dramatic purposes of the plays. Cornelius, in Cymbeline, for example, forms part of the dramatic machinery used to protect Imogen from a cruel death, thus affording an opportunity to develop and complete the plot.

A great many of these medical facts are expressed in the form of metaphor and simile. Although the use of the simile is especially frequent but few of these figures of speech are inaptly used. Many are sustained, consistent, and effective. Hotspur, in replying to Glendower's assertion that the earth shook when he was born, tells him that

> "Diseased nature oftimes breaks forth
> In strange eruptions; oft the teeming earth
> Is with a kind of colic pinch'd and vex'd
> By the imprisoning of unruly wind
> Within her womb; which, for enlargement striving
> Shakes the old beldam earth and topples down
> Steeples and moss-grown towers. At your birth
> Our grandam earth, having this distemperature,
> In passion shook."
>
> —*Henry IV*, Pt. I, III, I.

In the light of the gynecology of Shakespeare's day this figure is entirely consistent. One of the "Observations" of Dr. John Hall might also be quoted in corroboration of this, did the quaint phraseology permit.[1] "Wind in the womb" was a clinical entity in those days. The most sustained simile is that on the Belly and its Members in Coriolanus, which consists of thirty-two lines. Its inconsistency is explained by Menenius himself in pointing out that "The Senators of Rome are this good belly" and not the body politic, because . . . . "No public benefit which you" [the individuals composing the state] "receive

> But it proceeds or comes from them to you
> And no way from yourselves."

He concludes with the taunt

> "What do you think,
> You the great toe of this assembly?"
>
> —*Coriolanus*, I, 1.

The use of elaborate figures of speech might seem to presuppose a thorough knowledge of medicine. However, we must remember that the language of Shakespeare abounds in rich imagery. What remained bald medical facts in the hands of his literary contemporaries, Peele, Marlowe, and Greene; yes, or even rare Ben Johnson, was dressed in incomparable English by him. This is trite, I know, yet a quotation from Ben Johnson's Magnetic Lady (II, 1) will emphasize it:

> "He would keep you . . . . . not alone without a husband
> But in a sickness; ay, and the green sickness,
> The maiden's malady; which is a sickness,—
> A kind of disease . . . . .
> Give her vent
> If she do swell, a gimlet must be had;
> It is tympanites she is troubled with.
> There are three kinds: the first is anasarca,
> Under the flesh a tumor: that's not hers.
> The second is ascites, or aquosus,
> A watery humor; that is not hers neither;
> But tympanites, which we call a drum,
> A wind bombs in her belly, must be unbraced,
> And with a faucet or peg, let out
> And she'll do well: get her a husband."

These lines contain much medical lore but little poetry. How Shakespeare's genius would have transformed them! His was the magician's wand and he while

> "A thousand poets pried at life
> Alone rose to be Shakespeare."

If we compare the medical facts found in Coriolanus, Antony and Cleopatra, Julius Cæsar, Cymbeline, Lear, Macbeth, King John, and Henry VIII, it is impossible to distinguish one from the other. Coriolanus lived 430 B. C., Antony and Cleopatra and Julius Cæsar in 69 B. C.; Cymbeline and Lear in legendary England; Macbeth prior to 1056 A. D.; King John from 1199-1216 A. D., and Henry VIII from 1509-47. Consequently from Coriolanus to Henry VIII we have a period of 1977 years. Within this great period of time medicine, of course, went through various phases of develop-

[1] Cf. Aetius Chpt. XXXI. Diversum affectionum ob quas mulieres non concipiunt, curatio; also, Soranus, Chpt. LVI and LXXVIII.

ment. None of these phases is represented in the medical references in Shakespeare save as preserved in the superstitions and the medical lore of the common people and of physicians. It has been pointed out that the idea of the circulation of the blood given in Love's Labor's Lost is not as recent as that given in Coriolanus, and this fact has been used to show that Shakespeare must have kept abreast of the progress of medicine. Unfortunately for those who advance this argument, Menenius's words on the Belly and its Members have been traced to various non-medical sources which were undoubtedly accessible to Shakespeare. No attempt seems to have been made to harmonize the medicine with the time and scene of a play. The speech in which Timon enumerates so well many of the symptoms of secondary lues is a good illustration of this. Although Timon, the misanthrope, lived four centuries before the Christian era, yet he possesses the medical knowledge of the sixteenth century. A parallel to this is found in Hamlet, the thoughts and language of which are those of Christian England of the sixteenth century, while the scenes and characters belong to heathen Denmark of the twelfth century. Wherever, as in the case of the description of the apothecary's shop in Romeo and Juliet, there appears to be an adaptation, we find it to be mere coincidence and due to the sources from which the plays were taken. What is true of the language of Shakespeare is largely true of the medicine of Shakespeare. Both represent the England of Shakespeare.

Among the characters which possess a knowledge of medicine we find every walk of life represented. Doll, Mrs. Quickly, Pandolph, Falstaff, Boult, Speed, Biron, Leontes, Marcius, Ulysses, Iago, Friar Laurence, Holofernes, Warwick, Troilus, Titania, Brutus, Casca, Portia, Cleopatra, Cæsar, King Richard, Cerimon, Helena, Cornelius,—but where is the end? A motley procession. Libertine, wise-woman, servant, artisan, friar, schoolmaster, courtier, royalty, medical dilettant, and physicians,—all speak words of wisdom (?) on the great questions of health, of diseases and their cures, and of life and death. Those lowest in rank seem to have the greatest knowledge. Perhaps because theirs was the greatest need. No one takes more delight in airing his medical knowledge than the inimitable Falstaff. He is the man of the world and his is the experience of the world. It is he who knows about the treatment of *morbus gallicus* and he who expresses the most advanced ideas regarding contagion.

The medical knowledge of Shakespeare is held in common by all classes. There is no essential difference between what courtiers, kings, and queens know, and the medical knowledge of Doll, Mrs. Quickly, and Falstaff. The following quotations will serve to illustrate this point. Ulysses, the crafty politician and general, says:

> " . . . . . but when the planets
> In evil mixture to disorder wander,
> What plagues and what portents."
>
> —*Troilus and Cressida*, I, 3.

> " Be as a planetary plague, when Jove
> Will o'er some high-viced city hang his poison
> In the sick air: "
>
> —*Timon of Athens*, IV, 3.

rages Timon, a noble, in his pride.

When Hamlet's deportation to England has been decided upon the King says to his courtier Rosencrantz:

> " This sudden sending him away must seem
> Deliberate pause: diseases desperate grown,
> By desperate appliance are relieved,
> Or not at all."
>
> —*Hamlet*, IV, 3.

This opinion of cure by opposites is expressed also by Benvolio when he counsels Romeo for his love sickness, thus:

> " Tut, man, one fire burns out another's burning.
> One pain is lessen'd by another's anguish;
> Turn giddy, and be holp by backward turning;
> One desperate grief cures with another's languish:
> Take thou some new infection to the eye,
> And the rank poison of the old will die."
>
> —*Romeo and Juliet*, I, 2.

In his malediction on Prospero, the monster Caliban prays that

> " All the infections that the sun sucks up
> From bogs, fens, flats, on Prosper fall, and make him
> By inch-meal a disease! "
>
> —*Tempest*, II, 2.

Similarly, Titania laments:

> " Therefore the winds, piping to us in vain,
> As in revenge, have suck'd up from the sea
> Contagious fogs; which falling in the land
> Have every pelting river made so proud,
> That they have overborne their continents: . . . .
> Therefore the moon, the governess of floods,
> Pale in her anger, washes all the air,
> That rheumatic diseases do abound."
>
> —*Midsummer-Night's Dream*, II, 1.

Consumption is referred to by Falstaff, and Timon in the following words:

> " Consumption catch thee."
>
> —*Timon of Athens*, IV, 3.

> " Consumption of the purse . . . . . is incurable."
>
> —*Henry IV*, Pt. II, I, 2.

> " Consumptions sow
> In hollow bones of man."
>
> —*Timon of Athens*, IV, 3.

Rheum is spoken of by Iago, Polixenes, the French King, Pandarus, Aumerle, Anfidius, and others. Mandragora is mentioned by Iago and Cleopatra; henbane by Banquo and the Ghost; the pox by Iago, Speed, Katharine, and many others. It is needless to quote further or to multiply instances in which persons of widely different rank express similar medical knowledge. It is obvious that it would be impossible to learn the rank of the character from a given medical reference. Indeed it would be impossible to recognize the physicians themselves from the facts which they express. The three characters which show the greatest medical knowledge in a single utterance are not physicians, but laymen. Thersites,

the deformed Grecian slave, who plays the rôle of a fool, curses the Grecian commander, Patroclus, thus:

" . . . . . Now, the rotten diseases of the south, the guts-griping, ruptures, catarrhs, loads o' gravel i' the back, lethargies, cold palsies, raw eyes, dirt-rotten livers, wheezing lungs, bladders full of imposthume, sciaticas, limekilns i' the palm, incurable bone-ache, and the rivelled fee-simple of the tetter, take and take again such preposterous discoveries! "

—*Troilus and Cressida*, V. 1.

Biondello, a servant of Lucentio, knows almost as much about veterinary medicine as Thersites about the diseases of the South. Ichabod Crane and his broken-down plow-horse form scarcely a rival to Petruchio and

" his horse hipped with an old mothy saddle and stirrups of no kindred; besides, possessed with glanders and like to mourn in the chine; troubled with the lampass, infected with the fashions, full of wind galls, sped with spavin, rayed with the yellows, past cure of the fives, stark spoiled with the staggers, begnawn with bots, swayed in the back and shoulder-shotten; near-legged before and with half checked bit and a head stall of sheeps' leather which, being restrained to keep him from stumbling, hath been often burst and now repaired with knots; one girth six times pieced and a woman's crupper of velure which hath two letters for her name fairly set down in studs, and here and there pieced with pack thread."

—*Taming of the Shrew*, III, 2.

It is not necessary to say that a horse with all these diseases would not have been ridable! The haughty, immoderate, and reviling Timon, having lost all faith in his fellowmen, exclaims:

" Consumptions sow
In hollow bones of man; strike their sharp shins,
And mar men's spurring. Crack the lawyer's voice
That he may never more false title plead,
Nor sound his quillets shrilly; hoar the flamen,
That scolds against the quality of flesh
And not believes himself; down with the nose,
Down with it flat; take the bridge quite away
Of him that, his particular to foresee,
Smells from the general weal; make curl'd-plate ruffians bald;
And let the unscarred braggarts of the war
Derive some pain from you."

—*Timon of Athens*, IV, 3.

Some of the characters express what their prototypes said, or what is found in the sources from which the plays were taken. This is true of the cure wrought by Helena; of the cure of the King's evil in Macbeth; of the notion that a drug could be set like an alarm clock and could cease to act for " two and forty hours." This was taken from the Italian of Bandello, translated by Arthur Brooke.

" No pulse shall goe, no hart once beate within thy hollow breast,
But thou shalt lye as she that dyeth in a traunce."

—*Matteo Bandello—Romeus and Iuliet*, l. 2156.

The drugs spoken of in the plays of Shakespeare are chiefly such as were in daily use among the common people. Many of those that were not in use by them as home remedies were like familiar objects to them. Foxglove or digitalis, deadly nightshade or belladonna, hemlock or conium, henbane or hyoscyamus, and mandrake or mandragora all grew by the roadside. Some of these, as the " whoreson mandrake " were familiar largely because of the dread superstitions associated with them. Juliet refers to one of these in her fears of " So early waking " after taking the " distilled liquor " prepared for her by Friar Laurence,

" With . . . . . shrieks like mandrake torn out of the earth
That living mortals hearing them run mad."

—*Romeo and Juliet*, IV, 3.

The method by which the roots of this plant were obtained is shown in reprints of an illuminated manuscript. The figure shows two plants, to the leafy top of which a cord is fastened, the other end being tied to a dog's neck. In its struggles to free itself the dog was supposed to uproot the plant. These roots which were thought to have the human form are, strangely enough, represented by *male* and *female* figures. The poisonous character of monkshood or aconite were also known for centuries, although the therapeutic properties were not discovered until 1762. If we consider " cursed hebenon " or " insane root " to refer to the yew, then this too belongs among familiar plants. Nor is it at all unlikely that the virtues of " parmaceti for an inward bruise " or those of mercury at a time when the best surgeons still wrote " in laudem mercuriæ," were known to the laity. Falstaff surprises us, perhaps, by his enumeration of aphrodisiacs and by his entire familiarity with the customary treatment of lues. But why should not he know of both? It is he who knows all sorts and conditions of men and women. He has " hung loose " on the world, knows it at first hand, says what he thinks, and " blurts it out like a schoolboy." Moreover, if we compare Falstaff's knowledge of drugs with that of John Heywood's *Poticary* we shall be able to estimate it better. This *Poticary*, we recall, as one of the characters in " A newe and a very mery enterlude," a " playe called the Foure PP." When the Pedler, another of the Foure PP., asks:

" Then is that medycyn a souerayn thynge
To preserue a man from hangynge,"

the Poticary answers thus:

" If ye wyll taste but thys crome that ye se,
If euer ye be hanged, neuer truste me!
Here haue I diapompholicus,—
A speciall oyntement, as doctours discuse,—
For a fistela or a canker
Thys oyntement is euen shot-anker,
For thys medecyn helpeth one and other,
Or bryngeth them in case that they nede no other.
Here is syraups de Byzansis,—
A lytell thynge is i-nough of this,
For euen the weyght of one scryppull
Shall make you strong as a cryppul,
Here be others, as diosfiolios,
Diagalanga, and sticados,
Blanka manna, diospoliticon,
Mercury sublyme, and metridaticon,
Pellitory, and arsefetita,
Cassy, and colloquintita.
These be the thynges that breke all stryfe
Betwene mannes syckness and his lyfe;
From all payne these shall you deleuer,

And set you euen at reste for-euer.
* * * * * * * * * *
Not one thynge here particularly
But worketh uniuersally,
For it doth me as muche good when I sell it
As all the byers that taste it or smell it."
—*The Foure PP—John Heywood.*

Many of the remedies, such as cobweb, flax and eggs and keys for bleeding, were time-honored. This is true also of salve and heat for burns, plantain for broken shins, stewed prunes, a dry diet and tubs for those who had that in which, according to Lysimachus,

"A man may deal withal, and defy a surgeon."
—*Pericles*, IV, 6.

What has been said regarding the drugs and remedies applies likewise to most of the diseases, diseased conditions, and symptoms spoken of. To give a complete list would be tiresome. Among the commonest diseases we find rheums, agues, plagues, venereal diseases, leprosy, green-sickness, colic, spasms, "pin and web" or cataract, and "measles." The list of diseased states contains kibes or chilblains, boils, scars, carbuncles, fistula, abscess, gangrene, harelip, birth marks, fracture, dropsy, and others. Most of these, as well as such symptoms as the loss of appetite, and altered taste in disease; vomiting after surfeiting on sweets; obstruction of the blood by tight gartering; change of voice at puberty, were all known to "the general." Certainly no one having once seen the red cross with its accompanying legend "God have mercy on us" over the doorways of sealed houses containing the hopelessly sick and deserted patient, could ever forget the meaning of plague spots or "God's tokens" of death. The use of sputum, facies, pulse, and urine in the diagnosis of disease were daily occurrences in the life of physicians and of scores of those who were not physicians. Consequently we find various characters in the dramas speaking of their use.

The technical expressions are few, come from the lips of lay characters, and have in some cases been traced to non-medical sources which must have been familiar to Shakespeare. This is probably true of the expression *hysteria passio*. Other terms not so familiar to the tongues of men are: tent, of the surgeon; tremor cordis; pia-mater; serpigo; carbuncle; Carduus Benedictus; organ; function; cicatrix; abscess, and mandragora. It is very peculiar that when Shakespeare refers to the popular superstitions connected with the last-named plant he calls it mandrake, but when its therapeutic uses are spoken of he uses the term mandragora instead. Besides these technical expressions the truly wonderful delineations of madness, apoplexy, old age, and death have frequently been mentioned as showing that Shakespeare's medical knowledge as displayed in his plays was not only abreast, but in advance, of the state of the medicine of his day. The descriptions of madness found in the characterizations of Lear, Hamlet, Ophelia, and Lady Macbeth are familiar to everyone. It has been claimed that in his treatment of insanity by means of music, rest, and gentle conduct toward the patient, Shakespeare was several hundred years ahead of the physicians of his time. Be that as it may, for the present it is well to remember that many of the beggars who roamed the streets were madmen, and that the treatment of the insane, cruel beyond all description, might well awaken Shakespeare's compassion. They were bound, flogged, and cast into dungeons. Here they were chained, starved, and often made the objects of amusement for the nobility. Pitied by few, but most of all by Shakespeare in the touching words of Romeo:

"Not mad, but bound more than a madman is;
Shut up in prison, kept without my food,
Whipped and tormented, and—God—den, good fellow."
—*Romeo and Juliet*, I, 2.

Oh, the pathos of that ellipsis! As far as the delineations of insanity are concerned we must remember that it was customary to introduce mad-scenes into plays. Such are to be found in those of Marlowe, Green, and Peele. Not as good mad-scenes as those of Shakespeare, to be sure. Far from it. But they were not Shakespeares. Laehr in his "Darstellung krankhafter Geisteszustände in Shakespeare's Dramen" says that the conception of insanity and its origin in mental and bodily states was given Shakespeare, but that he was a far better observer and knew better how to apply his knowledge of disease than did his literary contemporaries. Laehr concludes as follows: "Uberall ergeibt sich also bei genauer Nachforschung, wie sehr sich Shakespeare in den wissenschaftlichen Anschauungen seiner Zeit bewegte, und wie gerade er das für seine Zwecke passende heraus zu greifen und zu beleben wusste."

We know that the company of players of which Shakespeare was a member had to leave London on several occasions because of the presence of the plague. Hence it is not surprising that it is often referred to. A few excerpts from Pepys' Diary may serve to recall its dreadful visitations. Although Pepys wrote of the great plague of 1663-5, the pictures of its earlier ravages are similar. On June 29, 1665, Pepys wrote:

"To White Hall, where the Court full of waggons and people ready to go out of town. This end of the town every day grows very bad of the plague."

July 12, 1665:

"A solemn fast day for the plague growing upon us."

July 30, 1665:

"It was a sad noise to hear our bell to toll and ring so often to-day, either for death or burials."

August 10, 1665:

"By and by to the office, where we sat all the morning; in great trouble to see the Bill this week so high, to above 4000 in all, and of them 3000 of the plague. Home, to draw over anew my will, which I had bound myself by oath to dispatch by to-morrow night; the town growing so unhealthy that a man cannot depend upon living two days."

August 31, 1665:

. . . . . "Every day sadder and sadder news of its increase. In the city died this week 7496, and of these 6102 of the plague. But it is feared that the true number of the dead this week is

near 10,000; partly from the poor that cannot be taken notice of, through the greatness of the numbers, and partly of the Quakers and others that will not have any bell ring for them. . . . . As to myself, I am very well, only in fear of the plague!" [Here we have an *estimated* mortality of 10,000 in a population of about 200,000, in a single week!]

September 6, 1665:

"To London, to pack up more things; and there I saw fires burning in the streets, as it is through the whole City, by the Lord Mayor's order. Thence by water to the Duke of Albemarle's; all the way fires on each side of the Thames, and strange to see in broad daylight two or three burials upon Bankside, one at the very heels of another; doubtless, all of the plague; and yet at least forty or fifty people going along with every one of them."

October 16, 1665:

"I walked to the Tower; but, Lord! how empty the streets are and melancholy, so many poor sick people in the streets full of sores; and so many sad stories overheard as I walk, everybody talking of this dead and that man sick, and so many in this place, and so many in that. And they tell me that, in Westminster, there is never a physician and but one apothecary left, all being dead; but that there are great hopes of a decrease this week; God grant it!"

October 29, 1665:

"In the street did overtake and almost run upon two women crying and carrying a man's coffin between them. I suppose, the husband of one of them, which methinks is a sad thing.

Shakespeare amidst such scenes, and then wonder at the frequent allusions to the plague! That would be doing scant reverence to his compassion and his genius.

The idea that the plague was due to a conjunction of the stars was still extant. This influence of the planets is spoken of by Ulysses when he says:

". . . . . but when the planets
In evil mixture to disorder wander,
What plagues and what portents,"
—*Troilus and Cressida*, I, 3.

In a treatise on the plague published by Lodge, in 1603, this idea is combatted, but the author falls into another fallacy by declaring on the authority of Avicenna that it is cured by an eastern hyacinth which is to be worn on the breast, or, preferably, is to be kept in the mouth. This hyacinth is also supposed to be able to resist all venoms. Autolycus in the Winter's Tale (IV, 4), referring to this custom of wearing charms against disease, declares: ". . . I have sold all my trumpery; not a counterfeit stone, not a riband, glass, pomander. . . ." Evidently Autolycus did not have the same faith in charms as Caius had in his kerchief. Besides the notion that the wind and the sun suck up disease from bogs, fens, and moors, and that the stars and planets "in evil mixture to disorder wander," we hear from the captain in Henry VI, Pt. II, IV, 1, that

"From their misty jaws (the jades)
Breathe foul contagious darkness in the air."

Among the agencies in the transmission of contagion the air holds first place. Consequently the Duke in Twelfth Night (I. 1) says of Olivia that "she purged the air of pestilence," and Portia pleads:

"What, is Brutus sick,
And will he steal out of his wholesome bed,
To dare the vile contagions of the night,
And tempt the rheumy and unpurged air
To add unto his sickness?"
—*Julius Cæsar*, II, 1.

That disease may be communicated by contact was not unknown to Shakespeare, for Falstaff tells us that

"Men take diseases one of another;
Therefore, let men take heed of their company."
—*Henry IV*, Pt. II, V, I.

We know that the clergy attributed morbus gallicus to divine visitation and that they were long accorded the benefit of their opinion after the laity were not. Astrologers naturally looked to the stars, but many physicians, notably Paré, took Falstaff's view (see Henry IV, Pt. II, II, 4). Physicians, crying in despair,

"'Tis contagious sickness;
Farewell all physick."
—*Henry VIII*, V, 2.

often fled before these epidemics, leaving their patients to the care of mountebanks or to those who gave baths. In such facts as these, rather than in the assertions that Shakespeare

"Did with unbashful forehead woo
The means of weakness and debility,"

lies the explanation for the many references to venereal diseases. The character of these references a personal perusal must reveal.

Among the therapeutic and diagnostic measures of the physicians of Shakespeare's time, purging, bleeding, and inspection of urine, or "water-casting," held a prominent place. They were frequently used to excess and are occasionally ridiculed in the plays of Shakespeare. In other instances their virtues are commended. Yet the picture presented to us by the many allusions, taken as a whole, agrees very well with that obtained by reading the professional literature of that day. Drastic purging was still practiced by the best physicians, but excessive bleeding and "water-casting" were not countenanced. Since it is much easier to obtain a good picture of the practices, as represented by Shakespeare, by direct quotations than by an attempted characterization, I shall adopt this method.

. . . "We are all diseased," (says the Archbishop in Henry IV),
"And with our surfeiting and wanton hours
Have brought ourselves into a burning fever,
And we must bleed for it."
—*Henry IV*, Pt. II, IV, 1.

The same advice is given by Biron in the lines:

"A fever in your blood! why then incision
Would let her out in saucers; sweet misprison!"
—*Love's Labor's Lost*, IV, 3.

According to Woodall's "Surgeon's Mate or Military and Domestic Surgery" a saucer or blood poringer held a trifle more than three ounces. Under the heading of "Blood Por-

ingers," Woodall cautions against too much bleeding as follows: "If the party be strong, except it be in case of Pleurisie, or some like urgent cause, I take less [than seven ounces]. I will rather offend in too little rather than in too much taking of blood away; for I have seen much hurt to have ensued by great quantity of blood taken away at one time." He also cautions against bleeding into basins as the German physicians did because of the inability of estimating accurately the quantity taken. This limit set by Woodall is but slightly exceeded by the First Sentinel in Coriolanus, when he threatens Menenius thus:

> "I say, go; lest I let forth your half-pint of blood."
>
> —*Coriolanus*, V, 2.

In the eighth of Dr. John Hall's "Select Observations on English bodies; or cures both empiricall and historicall performed upon very eminent persons in desperate diseases," etc., we find the following note:

> "Mrs. Chandler of Stratford-upon-Avon, aet. 38, after long sickness and great flux of her courses, was cured thus: (A drastic purge was first administered.) After being let blood her courses stayed to admiration, and she became well. Three years after, being extremely weakened with the like flux in the time of her lying in that death was expected, she was cured by bleeding."

King Richard's caution, "Our doctors say this is no month to bleed," (Richard II, I, 1) expresses well the popular superstition. People dared not be bled without consulting the stars. Those who could not pay for the services of astrologers consulted almanacs printed for that purpose. Even Queen Elizabeth herself had an astrologer in the person of Dr. John Dee, and the Rev. John Ward of Stratford-on-Avon, reports in his diary that "Nick Culpepper says a physitian without astrologie is like a pudden without fat." It is needless to say that the "puddin" usually contained fat.

In the sixteenth century to bleed meant also to purge. These were usually the initial procedures in case of fever and of many other affections. Macbeth, in speaking to the Scotch physician, bids him

> . . . . . "Cast
> The water of my land, find her disease
> And purge it to a sound and pristine health, ...
> Pull't off I say.
> What rhubarb, senna, or what purgative drug,
> Would scour these English hence?"
>
> —*Macbeth*, V, 3.

Purgation is usually spoken of in a figurative way as in this case. Other examples are:

> "Methought she purged the air of pestilence!"
>
> —*Twelfth Night*, I, 1.
>
> "Let's purge this choler without letting blood."
>
> —*Richard II*, I, 1.
>
> . . . . . "I
> Do come with words as medicinal as true,
> Honest as either, to purge him of that humour
> That presses him from sleep."
>
> —*Winter's Tale*, II, 3.

The nauseating character of the drugs used in general is repeatedly spoken of. That of those used to purge is likewise mentioned in the following homeopathic thought taken from the sonnets:

> "As to prevent our maladies unseen
> We sicken to shun sickness when we purge."
>
> —*Sonnet*, 118.

Hotspur, enraged at a certain dandy lord, contemptuously reports him as having said that

> "It was a great pity, so it was,
> [That] villainous saltpeter should be digged
> Out of the bowels of the harmless earth,
> Which many a poor fellow had destroyed so cowardly."
>
> —*Henry IV*, Pt. I, I, 3.

The exhausting nature of the excessive dosages of that time is brought out well by Coriolanus when he declaims against the assumption of popular rights after the people have disavowed him as consul. Coriolanus says that to assume these popular rights is

> "To jump a body with a dangerous physic,
> That's sure of death without it."
>
> —*Coriolanus*, III, 1.

The practice of prescribing from mere inspection of the urine had been so common that those who engaged in it were known as "water-casters" or "piddle doctors." This practice, which arose centuries before Shakespeare's time, resulted from restrictions upon the practice of medicine by monks, as a result of which they were no longer able to make personal visits to their patients. Hence they resorted to "water-casting." Treatises on "water-casting" seem to have been very popular. The "Urinal of Physik," written by Robert Recorde, who is usually credited with being the first English "piddle doctor," published in 1547, was reprinted in 1582, in 1599, and in 1665. This book, which in later editions went by the title, "The Judicial of Urines," gave pictures of the vessels used and subdivisions of urines with the prognoses in each case. In the Two Gentlemen of Verona, Speed apprises Valentine that . . . . "These follies are within you, and shine through you like the water in an urinal, that not an eye that sees you but is a physician to comment on your malady" (II, 1). Dr. Gideon Harvey, a physician contemporary with Shakespeare, quaintly describes a physician as giving the round toss to the urinal, or matula, to make the sediment subside. This urinal or matula was once the sign of the medical profession in Germany. One Notker, abbot of St. Gall in 1022, is said to have introduced the custom of having it carved on tombstones. Indeed, as late as 1450 Konrad von Sachsenhausen, the city physician of Frankfurt, had his tombstone similarly carved. Harris, in the Pharmacologia Anti-Empirica, tells of the impostures practiced by those who carried the specimens to the water-casters, and many amusing stories are told. He reports that Linacre, in order to show his contempt for the practice, often asked nurses and others to bring the shoe of the patient instead. One of the "quack" physicians, hearing of this, is said to have quickly proclaimed that he could diagnose and prognosticate all ailments from the odor of the shoe. As was the case with the

"piddle doctors," so also he undoubtedly did not always get the patient's shoe.

In Twelfth Night, III, 4, Fabian demurely advises Maria to "Carry his [Malvolio's] water to a wise woman" in order to determine whether Malvolio is bewitched or not. The value of this practice to the patient is probably estimated correctly by the page, who replies to Falstaff's question, "Sirrah, you giant, what says the doctor to my water?", with the words, "He said, sir, the water itself was a good healthy water, but for the party who owned it, he might have more disease than he knew for" (Henry IV, Pt. II, I, 2). Since, according to the Fifth Henry, chapter six, there were only twelve regular surgeons and probably a somewhat larger number of regular physicians in all London at the time of Henry VIII, it would be unjust to visit all this abuse on the regular "practisers of physic." As a class, physicians were, no doubt, urine inspectors. But a motley group composed the medical profession of that day. Since the London proper of Henry VIII had a population of about 150,000, it is evident that a few dozen regular doctors could not supply the need. Consequently there must of necessity have been many "irregulars." However, it would be unjust to conclude that all those who were not licensed by "the congregated college" were unsuccessful or even incapable practitioners. There are many evidences to show that the power of the Royal College of Physicians was for a time almost absolute and that it was sometimes arbitrarily used. But we have the testimony of Dr. Caius, the founder of Caius College and second president of the Royal College of Physicians, as to who composed the medical profession of that day. Dr. Caius enumerates "simple women, carpenters, pewterers, braziers, soap-ball sellers, apothecaries, and avaunters themselves," among physicians. Fifty years after this, Cotta, in his "Short Discoverie," gives a similar summary containing midwives, cooks, priests, witches, conjurers, jugglers, and fortune-tellers." Individuals were frequently licensed to practice specific things only, as for example, to cure fistula, extract or treat cataract, or to operate on hernia or hare-lip. However, the Royal College of Physicians made itself felt. The signs of physicians were to be displayed at their residences only and in consequence of a statute framed by Linacre, apothecaries were restrained from carrying the urine of their patients to a doctor and prescribing for the patient in consequence of the doctor's opinion. This statute was followed by another which forbade doctors to pronounce on any disorder from an examination of the urine alone.

We are all familiar with the freedom with which Shakespeare used Holinshed for the tragedies and historical plays. Whether it be the Palamon and Arcite of Chaucer which is to be transformed into the Two Gentlemen of Verona, the Tale of Troy which is to live again in Timon of Athens, or the Italian stories of Boccaccio and Bandello which are to be reinvigorated, we always find the master hand of Shakespeare moulding the crude materials of the sources according to the dictates of his unequalled dramatic genius. The same freedom taken with facts of history was taken with those of medicine. Many things have been adopted bodily, others have been greatly modified to suit the dramatic and artistic needs of the plays. Consequently we find anachronisms, inaccuracies, exaggerations, and contradictions.

"A letter for me?" asks Menenius, "It gives me an estate of seven years' health, in which time I will make a lip at the physician; the most sovereign prescription in Galen is but empiricutic, and, to this preservative, of no better report than a horse drench" (Coriolanus, II, 1). Coriolanus lived four to three hundred years before Galen. Hence Menenius could hardly make a lip at Galen. Besides these words are not characteristic of the times. To "make a lip at Galen" was not the attitude of Shakespeare's time, even if a layman might have done so with impunity. Not so a physician, however. This is shown by the following entry from the Roll of the Royal College of Physicians, of London (2d Edition, Vol. I, p. 62, 1878): "On his acknowledgment of error and humble recantation, signed with his own hand, he was received into the College." The person disciplined was Dr. John Geynes, who was cited before the College in 1559 for impugning the infallability of Galen. This was but fifty years before Coriolanus was written.

"Who keeps the tent now?" asks Patroclus of Thersites. The reply is, "The surgeon's box or the patient's wound." The time of the tragedy of Troilus and Cressida is 1184 B. C. Consequently we do not expect to hear of a surgeon's box or of the use of a tent. A similar anachronism is the use of the doctor's title in Macbeth several hundred years before the time in which it came into use. Other errors are the use of the kerchief of Shakespeare's day with its medical significance in the Roman times of Julius Cæsar, and the presence of symptoms of quickening by the second month. Little significance should, however, be attached to these errors. Many may be intentional. Besides we must allow for poetic license. These things must be regarded as we regard the introduction of cannon in King John and in Macbeth. This made the warfare of these plays more intelligible.

Instances of extravagant expressions are numerous, and are frequently accounted for by the dramatic situation or the character of the speaker. No one would take Fabian seriously when he implies that he can tell a madman by inspecting his brain; or Hamlet, when he determines the question of his sanity by the state of his pulse; or the King in All's Well That Ends Well, when he says that Helena has repealed the banished sense of his hand. Other examples are Gloucester's assertion that he was born with teeth; Helena's cure in two days of a fistula which the "congregated college" had declared incurable; and Lafeu's boast that he has "seen a medicine"

> "That's able to breathe life into a stone,
> Quicken a rock, and make you dance canary
> With sprightly fire and motion."
> —*All's Well That Ends Well*, II, 1.

In this class of references we must also place the threat of ovariotomy by the irate Antigonus in the Winter's Tale, II, 1.

We must not take these things literally any more than we take Shakespeare literally when he makes Romeo declare, "Hang philosophy unless philosophy can make a Juliet." Indeed, if we take everything in the plays of Shakespeare literally, we rob the great Linnaeus of the discovery of sex in plants, for, in the Winter's Tale, Perdita speaks of . . . . "pale primrose that die unmarried." This apparent reference to sex recurs more clearly in Romeo and Juliet and in Midsummer Night's Dream in the following words:

"Among fresh female buds
Shall you this night inherit at my house,"

and

"The female ivy that enrings the barky fingers of the elm."

I am fully aware that there are those who have magnified Shakespeare's insight until they have claimed that he foresaw advancements in science which only the great scientists of the twentieth century have achieved. Such assertions, however, are interesting mainly as an index to a large part of the literature on this subject. It would be doing a great wrong to the truly learned physicians and surgeons of the sixteenth century and to their illustrious predecessors, to claim that the characteristics of the medicine of the plays of Shakespeare are those of the medicine of Woodall, Riolan, Botal, Harvey, Caius, Banester, Linacre, Paré, and many others. There are, it is true, some points of similarity, yet little can be found in the medicine of the dramas of Shakespeare indicative of the learning of these men. It is the popular, and the general rather than the special and minute, that is found in Shakespeare. The picture we obtain is, in the main, that which could easily be obtained from the life of that time by a layman of *such extraordinary genius* as Shakespeare's. The wonderfully accurate descriptions of death and old age are eloquent testimonials of his powers of observation, expression and portrayal. It would be useless to try to find parallels to them in the professional treatises of that time or of any other time. Be their professional attainments what they might, lacking Shakespeare's genius, physicians were, and must remain, unable to write as wrote the great master of English. To be sure, there are certain internal evidences tending to show that the medicine of the plays of Shakespeare is, in some things at least, fully abreast of that of the professional treatises of the times. But they are too few and inadequate to characterize it as a medicine based on clinical experience and anatomical knowledge. In short, the medicine of the plays of Shakespeare is Hippocratic medicine modified by Galenism, with a touch of Paracelsus. These elements are all represented in the best treatises on medicine of the sixteenth century. The characteristics of the medicine of Shakespeare are, in a manner, those of the medicine of the best physicians contemporary with him. It is not, however, a purposeful medicine based on medical training and clinical experience, but incidental, the product of a world genius, and therefore a greater tribute to his enduring fame.

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[2] All references to the plays of Shakespeare are based on the International Edition of the University Society of New York. Only a partial list of references to the literature on the medicine of Shakespeare has been given.

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THE VARIOUS TYPES OF CARCINOMA CERVICIS UTERI: THE CHANGES THEY UNDERGO WITH THE PROGRESS OF THE DISEASE AND THEIR CLINICAL SIGNIFICANCE

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Experience has taught us that the clinical course of cancer of the uterine cervix is usually rapid; the patients rarely live over three years, about three-quarters of them die within two years, and one-third within one year, after the first manifestation of the disease. Bleeding in some form is usually the first evidence of this condition; this is sometimes not present until late in the course of the disease, but if absent, usually some other symptoms such as a watery or foul discharge should call attention to the growth. In a small percentage of the cases all symptoms referable to the growth are absent until after it has extended beyond all possibilities of a cure. Bleeding or a blood-tinged discharge was present in about ninety-three per cent of 412 cases of cervical cancer admitted to Dr. Kelly's clinic at the Johns Hopkins Hospital, and in over sixty per cent of these cases there was a history of neglected uterine bleeding for over six months. When we bear in mind the usual rapid course of the disease, we can readily understand why hysterectomy so seldom cures this condition, why it is important to make an early diagnosis and also why the patient should be operated upon as soon as possible after making this diagnosis.

We know that only a small percentage of all cases have been "operable," and we also have learned that a small percentage of those operated upon can be cured, but believe that all could be cured if the entire diseased condition could be removed and implantation avoided. The importance of an early diagnosis is very urgent, and fortunately it is possible in a large percentage of the cases if women only realized the curability of this condition in its early stages and we, the physicians, would ascertain without delay, in every instance, the cause of uterine bleeding or of any other symptom referable to the uterus.

Two things then are very essential; first, the education of women along these lines, and second, our own education in order that we may better understand the pathological changes caused by this disease and their clinical manifestations.

All women should fully realize that any uterine bleeding or other symptoms referable to the pelvic organs may be indicative of some slight trouble, which may not need any attention or can be easily remedied if it does, or on the other hand, that it may be the first manifestation of cancer which, if operated upon in its incipiency, should be cured in a large percentage of the cases. This bleeding may be slight, "only a show" appearing at irregular intervals as on exertion, or after coitus, or after using a douche or straining at stool. In other cases the bleeding may be slight but constant, the patient noticing that her clothes are slightly soiled on taking them off at night. Sometimes the bleeding is more profuse, so that it may appear like a prolonged menstruation, an irregular menstruation or a return of the flow after the menopause. In still other cases there may be severe hæmorrhages.

All physicians should bear in mind that there are various types of the growth which may alter the clinical picture of the disease, and the various stages of each type may also present different clinical features.

It seems appropriate to study these various types and the changes they undergo during the progress of the disease, in order that we may understand the clinical manifestations of the disease, its diagnosis and the indications for its treatment.

While Resident Gynecologist at the Johns Hopkins Hospital, I began a careful study of twenty-seven specimens removed by the more radical abdominal operations and also one autopsy specimen from a patient with cervical cancer, dying from cerebral embolism due to an acute endocarditis. Fortunately only a few of these cases had been curetted and an excellent opportunity presented itself to study the various types and the changes they undergo as the disease progresses. A drawing, to measure, was made of each specimen removed and also one of the vaginal portion of the cervix and in several instances plaster casts of the latter were made. The specimens were hardened in 4 per cent formalin and, after hardening, a sagittal slice about 2 mm. in thickness was removed, thus dividing the specimen into two halves. This slice (either as a whole or else divided if too large) was imbedded in celloidin, cut and stained as a microscopical section, thus giving a stained sagittal section of the entire uterus, demonstrating the relation of the disease to the cervix and its method of extension through the tissues of the cervix, and in a few instances into the fundus. Cross sections were then made of each half of the specimen and by this incomplete series the invasion of the parametrium was studied. From the sagittal sections and the series (incomplete) of cross sections, the growth was reconstructed thus demonstrating its relation to the parts involved. Cancer was either found or its existence excluded from the pelvic lymph nodes removed.

Here I wish to thank Dr. Kelly for the use of this material from his Clinic and also for the use of the eight drawings bearing Mr. Broedel's name, which were made for the second edition of Dr. Kelly's Operative Gynecology. I also wish to

thank Mr. Broedel for the aid he kindly gave me which enabled me to make the other illustrations.

CLASSIFICATION OF CANCER OF THE UTERINE CERVIX.

I. *Histological.*—The vaginal portion of the cervix is normally covered by stratified epithelium which is directly continuous with that of the vagina and usually ends at the external os but may extend up into the cervical canal for varying distances, which is especially true as women grow older. The cervical canal, on the other hand, is lined by high cylindrical cells which generally meet the stratified epithelium at the external os, but may extend over the vaginal portion of the cervix. Cancer arising from the stratified epithelium, no matter the place of origin, whether from the vaginal portion or within the cervical canal, is known as *squamous cell carcinoma.* Likewise cancer arising from the cylindrical epithelium or glands of the cervix, no matter its place of origin, is known as *cylindrical cell* or *adeno-carcinoma.*

II. *Topographical.*—As we may group all forms of uterine cancer according to whether they arise in the body or in the cervix, in like manner we may classify cervical cancer according to its origin whether in the *vaginal portion* of the cervix, or within the *cervical canal.*

III. *Morphological.*—Irrespective of the situation of the growth or its histological structure, we may group it according to its morphology. We do not know why, in one case, the growth seems to "evert" giving rise to a papillary or cauliflower mass, or in another, apparently the same type of growth may "invert" forming a nodule or mass of cancerous tissue in the cervix with but very little evidence of the disease on the surface. The malignant process may be circumscribed in one instance, and apparently the same type of growth may be diffusely scattered throughout the cervical tissue in another. Intermediate forms and sometimes both processes are present in the same specimen. Apparently in the progress of the disease the growth may sometimes pass from one morphological type into the other. We can, however, frequently make the following classification:

1. Everting or vegetative (synonyms—cauliflower, papillary and proliferating);

2. Inverting or infiltrative (synonyms—nodular, ulcerative and parenchymatous).

In some cases the cancer cells predominate and the stroma forms a very small part of the tumor, as a result the tumor may feel soft, hence the term *medullary,* and it may early become necrotic and portions of it slough away. The process less frequently invades the cervical tissue in a diffuse manner forming a growth in which the stroma predominates, the so-called "scirrhus" cancer, which may retain its form for a long period of time. Specimens are encountered which cannot be included in the above classification and which should be looked upon as "exceptions" or isolated cases until we learn more about them and either discover, on further study, that they belong in one of the above groups, or that it may be necessary to form new groups for them.

The following groups of cases will be considered:

I. Squamous cell carcinoma; (1) Vaginal portion of the cervix; (a) everting, (b) inverting; (2) Cervical canal; (a) everting, (b) inverting.

II. Cylindrical or adeno-carcinoma. Sub-classification as above.

Squamous Cell Carcinoma—Vaginal Portion of Cervix—Everting or Vegetative.

This type of growth apparently begins as a proliferation of the epithelium of the vaginal portion of the cervix and, associated with this, there is a reaction of the deeper cervical tissue giving rise to a papillary outgrowth into the vagina, which consists of a central core of vascular connective tissue covered by the proliferated epithelial cells. This outgrowth may arise from any portion of the vaginal portion of the cervix and may form either a pedunculated or a sessile tumor. As the disease progresses the tumor increases in size, either spreading over the surface of the vaginal portion of the cervix, or over the vaginal walls or up the cervical canal, and it may partially or completely fill the vagina. At the same time the deeper tissues are invaded. In one case there may be an enormous mass filling the vagina with but little extension of the disease into the deeper tissue, and in another case the external manifestation of the growth may be small, while its extension into the deeper tissues may be great. Figs. 1 and 2 illustrate one of these growths which has involved the posterior cervical lip and is gradually absorbing the deeper tissues, spreading over the vagina posteriorly and invading the cervical canal by replacing its mucosa. It has extended about one-third the way up the canal and in places has occluded the openings of the cervical glands, thus causing retention cysts. Figs. 3 and 4 illustrate another case where the entire vaginal portion of the cervix is involved and the growth is beginning to invade the deeper tissues at the junction of the vagina and posterior cervical lip. This is probably the least malignant of the various forms of cervical cancer. The external evidence of the disease may suggest a very advanced case and there may in reality be but very little extension of the disease. One would infer that bleeding would occur early in the course of the disease in this group of cases and probably this is true. Both cases, represented here, had been bleeding for over five months before the operation. The situation of the growth on the vaginal portion of the cervix and its morphology renders its detection, on palpation or inspection, comparatively easy. Unfortunately this group probably occurs less frequently than the following group which is more malignant and difficult to diagnosticate.

Squamous Cell Carcinoma—Vaginal Portion of Cervix—Inverting or Infiltrating.

The inverting or infiltrating type also apparently begins as a proliferation of the epithelium of the vaginal portion of the cervix, and here the papillary formation is absent or plays a minor part. The growth seems to invert itself into the

tissues of the cervix and usually gives rise to a more or less circumscribed mass of cancerous tissue. Usually the stroma plays a small part in the structure of the tumor and the epithelial cells predominate, the so-called medullary cancer; less frequently, however, the disease process invades the cervical tissue in a diffuse manner forming a growth in which the stroma predominates, the so-called scirrhus cancer. The starting place of the new growth varies in different cases. In the one shown in Figs. 5 and 6, it apparently started in the centre of the anterior lip near the junction of the squamous and cylindrical epithelium, while in the case shown in Figs. 7 and 8, it apparently started in a similar place of the posterior lip. On the other hand, in the case shown in Figs. 9 and 10 there is possible a double focus, *i. e.*, the simultaneous appearance of the growth in each angle of the external os.

As the disease progresses it invades the deeper tissues of the cervix, extending directly in and usually avoiding the cervical canal. Sometimes a large mass of cancerous tissue will be found, hence the name "nodular cancer." In the specimen shown in Figs. 5 and 6 the entire anterior wall of the cervix had apparently become involved before ulceration had taken place. More often, however, the processes of invasion, necrosis and ulceration go on together as shown in Figs. 7, 8, 9, 10, 11, and 12, hence the term "ulcerative" cancer. As the disease progresses further and replaces the tissues of the cervix, the central core including the cervical canal frequently sloughs away and the cervix is converted into a crater-like cavity lined by necrotic cancerous tissue as shown in Figs. 13 and 14. The clinical manifestations of this type depend on the amount of necrosis and ulceration. A growth which becomes necrotic early in its course would give rise to symptoms sooner than one which did not. In the patient shown in Figs. 5 and 6, where there was an extensive cancerous mass with but very little necrosis, bleeding had been noticed but seven weeks before the operation, while in the one shown in Figs. 9 and 10 bleeding had been present for over eight months. Yet in the latter case the growth was small and without metastases, while in the former, the growth was large and metastases had occurred. We must infer, that in the patient with a small growth and symptoms for eight months either the disease progressed very slowly or the symptoms appeared very early, and in the other with a large growth and bleeding for only seven weeks, either the cancer grew very rapidly or else the symptoms did not appear until late. The patient, whose uterus is shown in Figs. 7 and 8 had known of the ulcerated condition of the cervix for six months and yet one sees that the primary growth was very small; on the other hand, metastases to the pelvic lymphatics had already occurred. In the case shown in Figs. 11 and 12 the diagnosis was made on examining the patient for symptoms arising from a pelvic inflammatory disease which was associated with the cancer, but independent of it, and symptoms referable to the cancer had been of but ten days' duration. The disease had metastasized at the time of the operation and the patient later died from recurrence due to some of the cancerous pelvic lymph nodes which had not been removed at the operation. On the other hand, the uterus shown in Figs. 13 and 14 had been bleeding for over six months before the operation.

It can readily be seen in this type of cancer, that if the growth is rapid or necrosis is delayed the disease may easily pass beyond the curative stage before it is detected. On the other hand, if the growth is slow and especially if necrosis occurs early, the diagnosis may be made while the disease is still local. *Unfortunately there is no relation between the extent of the diseased process and the duration of the symptoms, i. e.,* the disease may be extensive and the symptoms of short duration and also the disease may be early and it may have manifested itself, clinically, for a long time.

In the further progress of the disease the bladder may be involved anteriorly as shown in Fig. 15 and later a vesico-vaginal fistula may appear. In the posterior extension of the disease the cul-de-sac may become obliterated and the rectum become invaded as shown in Fig. 16 or the rectum may become invaded through the posterior vaginal wall. As a result of the posterior extension of the disease a recto-vaginal fistula may appear. In the lateral extension of the disease the ureters soon become surrounded and compressed, or if it extends both posteriorly and laterally, the sciatic nerves may become invaded and cause excruciating pain. Fortunate indeed is the woman when the ureters become compressed before the formation of the above mentioned fistula or invasion of sensitive nerves, for the resulting renal insufficiency benumbs the sensibilities and favors a terminal infection.

It can be seen that the inverting or infiltrating variety is more malignant than the everting type and is also of more frequent occurrence. Unfortunately it may not give rise to any symptoms until after it has extended beyond the uterus. Its detection by inspection or palpation, unless ulceration is present, is also more difficult than in the everting type.

Squamous Cell Carcinoma—Vaginal Portion of Cervix—Both Everting and Inverting.

As has been previously stated, both types of growth may be present in the same specimen and in fact usually are, for the one name or the other is given to the prevailing type. We have papillary projections from the floor of the ulcer or sides of the craterous cavity and every everting type eventually has an infiltrating base. So the classification is somewhat artificial, but is of importance as a help in understanding the various forms of growth. In the case shown in Figs. 17 and 18, which probably belongs in the last group mentioned, the disease apparently began as an infiltrating form but burst its outer shell and assumed the everting type. This patient had been bleeding for three months. Notice that the growth apparently began in the posterior lip, invaded the deeper tissue and through it encircled the cervical canal.

Squamous Cell Carcinoma—Cervical Canal—Everting.

Squamous cell carcinoma arising within the cervical canal

may also be grouped into the everting and inverting forms; the everting form may fill the canal or even protrude through the external os into the vagina. In Figs. 19 and 20 is shown the shrunken and retracted cervix so characteristic of the growths developing in the cervical canal and in addition a portion of the growth is protruding from the external os as a papillary outgrowth. The sagittal sections show that a pyometra had resulted from the occlusion of the cervical canal by the growth. This is the only instance in the twenty-eight cases where there was any resemblance to an everting type of growth arising from the cervical canal. A history of three months' bleeding was present and the growth had invaded the parametrium, and metastases were found in the pelvic lymph nodes.

Squamous Cell Carcinoma—Cervical Canal—Inverting.

The same changes occur in the inverting type of growth starting in the cervical canal as in the similar type of growth arising from the vaginal portion of the cervix. However there is this difference. This form of growth, arising from the vaginal portion of the cervix, nearly always extends by invading the deeper tissue of the cervix rather than spreading over the mucous membrane and up the cervical canal; as a result the cervical canal may be entirely surrounded by cancer and yet remain intact until late in the course of the disease, and finally the central core including the canal may slough away. On the other hand, in cancer arising within this canal the mucosa of the canal is the first tissue attacked. From the mucosa, the cancer spreads on all sides into the cervical tissue. We nevertheless see the changes caused by infiltration and ulceration, and finally the cervix is converted into a thin shell lined by cancerous tissue just as in the other type. In the advanced stages the picture may be such that it is impossible to state whether the disease started within the canal or from the vaginal portion of the cervix. Frequently, however, the vaginal portion of the cervix may not be invaded—even in cases of extensive cancer developing within the canal (see Figs. 25 and 26). In Figs. 21 and 22 is shown a very early case in which the disease had started within the external os and after spreading over the surface of the cervical canal, had invaded the deeper structures on all sides, and yet there has been but little change in the vaginal portion of the cervix. A little puckering of the anterior lip, caused by the lower edge of the growth just within the external os, was present. In the specimen shown in Figs. 23 and 24 the disease is further advanced, more of the cervical tissue has been invaded and also the tissue beneath the mucosa of the vaginal portion of the cervix, thus causing a retraction and puckering of the latter. The specimen shown in Figs. 25 and 26 represents a still further stage of the disease where the entire central portion of the cervix had sloughed away. Note, however, that there has been but very little involvement of the vaginal portion of the cervix, the latter being retracted, shrunken, and puckered, but its mucosa, for the most part, is intact.

In the specimen shown in Figs. 27 and 28 the growth had invaded the cervical tissues in a diffuse manner, the so-called scirrhus type, and had undermined the mucosa covering the vaginal portion of the cervix causing the former to slough away from the greater portion of the cervix, there still being an irregular border of intact mucosa about its outer margin. The growth had also invaded the deeper tissues of the vagina on all sides of the cervix without involving its mucosa.

The symptomatology varies in these cases and there is no definite relation between the duration of the symptoms and the extent of the disease. In the very early case shown in Figs. 21 and 22 a thin watery discharge had been present for three years, and bleeding was first noticed only a few days before the patient came to the hospital. The patient represented in Figs. 23 and 24 had been bleeding for seven months, and the one represented in Figs. 25 and 26 had been bleeding for eighteen months, but here a uterine polyp was found which may have also caused bleeding. Bleeding had been present for two and a half years in the patient represented in Figs. 27 and 28.

The diagnosis of this type presents all the difficulties of the preceding one, with the additional feature that the disease starts within the cervical canal. The disease seems, rarely or only very late, to appear on the vaginal surface of the cervix. However, there is one very important feature which aids in the diagnosis and that is the alterations in the vaginal portion of the cervix caused by the disease invading its deeper tissues. The vaginal portion of the cervix becomes indurated, and with necrosis, the cervix becomes retracted, puckered, and the vaginal mucosa covering it, is thrown into folds. This induration, retraction, and puckering of the vaginal portion of the cervix is as characteristic of this form of cancer, as is the retraction of the skin or the nipple characteristic of the mammary cancer lying beneath. The prognosis in these cases is probably about the same as in the similar type arising from the vaginal portion of the cervix.

Squamous Cell Carcinoma—Inverting—Starting Place Undetermined.

In very advanced cases it may be impossible to determine the origin of the growth. In the two specimens shown in Figs. 15 and 16 the disease apparently started from the vaginal portion of the cervix and not from within the canal, still this cannot be definitely stated. As previously emphasized, it is remarkable how extensive the disease may be in a growth starting within the canal and the vaginal portion of the cervix may not yet have been destroyed. In the specimen shown in Figs. 29 and 30 it is impossible to definitely state the origin of the growth (classified under inverting type arising from the vaginal portion of the cervix), whether from the vaginal portion of the cervix, the vagina, or just within the external os. There was a marked reaction on the part of the surrounding tissue causing an infiltration of eosinophiles, so marked as to greatly obscure the malignant growth. As shown, the cervix and vagina are both involved; in addition

the parametrium was invaded by direct extension and by metastases, and metastases were present in the pelvic lymph nodes. The bleeding was of six months' duration.

Adeno-Carcinoma—Uterine Cervix.

This, as we know, may arise from the vaginal portion of the cervix or from within the cervical canal and may be everting or inverting. The specimen shown in Figs. 31 and 32 now appears as an infiltrating type starting within the cervical canal. There was a history of bleeding for seventeen months, and seven months before her admission to the hospital a tumor was removed from the cervix. This suggests that there was probably present, at that time, a fungating growth protruding from the external os, *i. e.*, it originally manifested itself as an everting type arising from the cervical canal. In Figs. 33 and 34 is shown a specimen of adeno-carcinoma obtained at autopsy, the patient died of cerebral embolism from acute endocarditis. Metastases were found in the lungs, liver, and in the thoracic, abdominal, and pelvic lymphatics. There was a history of bleeding for six months. The growth is apparently of the inverting type starting from the deep cervical glands, as the mucosa lining the canal was normal in places. It may have originated in the left corner of the vaginal portion of the cervix, but this does not seem probable. In Figs. 35 and 36 is represented a third case of adeno-carcinoma of the inverting type starting within the cervical canal and causing occlusion of the canal, with a resulting pyometra. The retracted puckered cervix is well shown, and this is covered by epithelium having the histological appearance of squamous cell carcinoma, thus suggesting the presence of both adeno-carcinoma and squamous cell carcinoma in the same specimen. There was a history of bleeding for seven months

Figs. 37 and 38 represent a specimen of apparent adeno-carcinoma starting within the cervical canal and suggest a double focus. The growth was apparently very early, symptoms of bleeding having been manifest for only three weeks. It, however, recurred in a few months after the operation and soon filled the pelvis. The recurrence manifested itself first in the vaginal vault and suggested that an implantation of cancer cells had taken place during the operation.

THE CLINICAL SIGNIFICANCE OF THE VARIOUS TYPES OF GROWTHS.

The following classification of cancer of the uterine cervix has been made:

I. Histological: (1) Squamous cell carcinoma. (2) Cylindrical cell or adeno-carcinoma.

II. Topographical: (1) Those arising in the vaginal portion of the cervix. (2) Those arising in the cervical canal.

III. Morphological: (1) Everting or vegetative (synonyms —cauliflower, papillary, and proliferating). (2) Inverting or infiltrating (synonyms—nodular, ulcerative, and parenchymatous).

In the majority of the cases we can employ the above classification. The histological picture is usually definite, but at times the diagnosis may be in doubt; in the case shown in Figs. 35 and 36 both adeno-carcinoma and the squamous cell variety are present. A difference of opinion has been expressed by different pathologists as to the diagnosis in Figs. 37 and 38. The topographical diagnosis is not always evident. It is remarkable how extensive a growth, arising from the vaginal portion of the cervix and invading the deeper tissues of the cervix, may be, and yet the cervical canal may be intact or very little involved, as shown by the sagittal sections in Fig. 12. Likewise one may have a very advanced growth arising within the cervical canal and the vaginal portion of the cervix may be intact, or slightly involved, or else invaded only from the deeper cervical tissues (see Figs. 14 and 16). However, in many of the very advanced cases it is impossible to state where the growth arose and the same is true of a few of the early or operable ones. In considering the morphology of the growth some are definitely everting, as shown in Figs. 1, 2, 3, and 4, and others are just as definitely inverting as shown in Figs. 5, 6, 7, and 8, but in others both processes may be present in the same specimen and also, in the progress of the disease, the growth may pass from one type to another.

The Clinical Significance of Squamous Cell Carcinoma—Vaginal Portion—Everting.

Four of the twenty-eight specimens were of this variety and possibly one or two others included in the next group. In only one of the four cases was the parametrium involved by cancer and in two of the cases, in which the pelvic lymph nodes were studied, cancer was not found. In one of the four cases there was a history of neglected uterine bleeding for over six months and in the other three for over five.

The above suggests that this is one of the most favorable types of growth, invading the surrounding tissue slowly and soon giving rise to symptoms. It is so situated and of such an appearance and structure that it may be easily diagnosed on inspection or palpation.

The Clinical Significance of Squamous Cell Carcinoma—Vaginal Portion—Inverting.

This is apparently the most frequent type of the squamous cell variety, occurring fifteen times in the nineteen cases of cancer arising from the vaginal portion of the cervix. It is apparently as malignant or even more malignant than the same variety arising within the canal, for it spreads by directly invading the deep tissues of the cervix rather than by extending over the surface, as up the cervical canal or over the vagina. It also soon reaches the parametrium, and metastases may occur even before the latter has become invaded by the tumor. The parametrium was involved, either by direct extension or metastases, in eleven of the fifteen cases. Some of the lymph nodes were studied in fourteen cases and were found involved in six, and in two of these six cases no evidence of cancer was found in the parametrium. In seven of

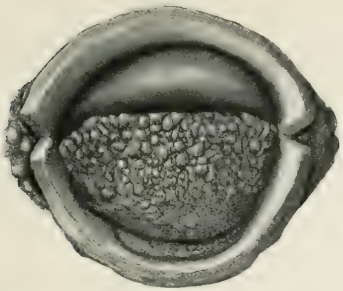

FIG. 1.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix, Everting or Vegetative (Gyn. Path. No. 7601).

Patient 37 years old; 4 children (youngest 9 years). A bloody discharge had been present for five months and a severe hæmorrhage occurred, while straining at stool, three weeks ago. Pain was probably due to adhesions from pelvic inflammatory disease. General condition was excellent.

The movements of the uterus were limited by pelvic adhesions from a previous pelvic inflammatory disease. The parametrium was apparently free.

Vaginal portion of the cervix (natural size) shows that the posterior cervical lip has been replaced by an everting papillary growth which bled on palpation. The growth had begun to spread over the posterior vaginal wall.

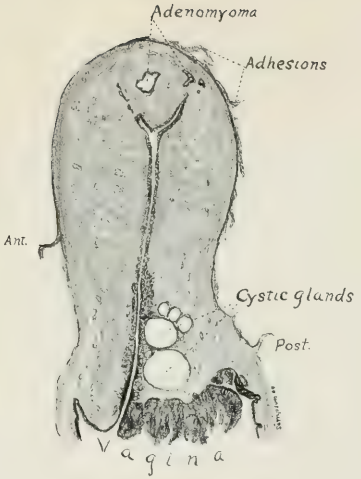

FIG. 2.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 1.

The papillary growth is gradually absorbing the tissue of the posterior cervix lip and is beginning to spread over the posterior vaginal wall and up the cervical canal occluding the openings of some of the cervical glands, and thus causing retention cysts.

The adhesions are shown on the surface of the uterus and an adenomyoma is present in the fundus. Cancer was not found in the parametrium or in the pelvic lymph nodes removed.

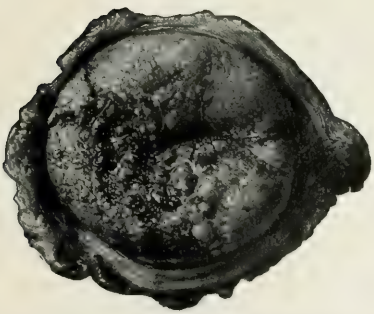

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FIG. 3.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix, Everting or Vegetative (Gyn. Path. No. 8155).

Patient 30 years old; 1 child (15 years). More or less constant bleeding had been present for five months, and was the only symptom. General condition was excellent.

The uterus was freely movable and parametrium was apparently normal.

Vaginal portion of the cervix (natural size) shows that both lips have been replaced by an everting papillary growth which bled easily, on palpation.

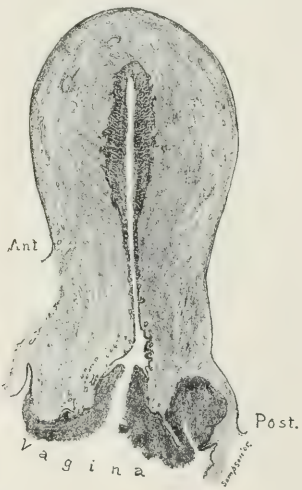

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FIG. 4.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 3.

The papillary outgrowth has covered the entire vaginal portion of the cervix and has invaded the deeper tissues at the junction of the posterior lip and the vagina. Cancer was not found in the parametrium (the pelvic lymph nodes were not removed).

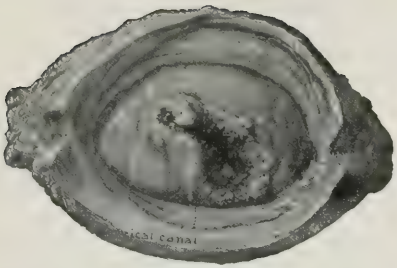

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FIG. 5.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting or Infiltrating (Gyn. Path. No. 6669).

Patient 62 years old; 2 children (45-43 years); menopause nine years ago. Bleeding at irregular intervals had been present for seven weeks, usually when straining at stool and at one time amounting to a severe hæmorrhage. A very profuse watery discharge, not offensive, had been present for four months. Pain was not present. General condition was poor, hæmoglobin 68 per cent.

Uterus was freely movable and parametrium apparently normal.

Vaginal portion of cervix (natural size) shows a markedly hypertrophied and indurated anterior cervical lip, the center of which has broken down, forming an ulcer lined by friable necrotic tissue, the posterior lip has become atrophied and the canal displaced backwards.

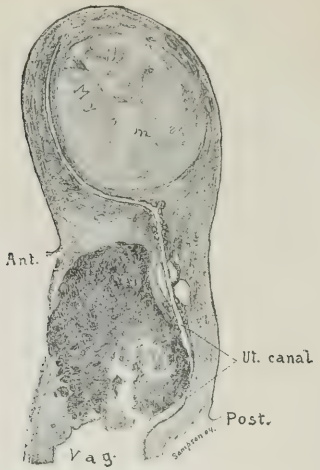

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FIG. 6.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 5.

The growth has formed a mass of cancerous tissue involving the anterior wall of the cervix and extending as high as the internal os. Note that the cervical canal has just begun to be involved and that it has been displaced backwards and that the fundus, vagina, and posterior wall are free. A submucous myoma is present in the posterior uterine wall.

A metastasis was found in a parametrial lymph node, the pelvic lymph nodes removed were free.

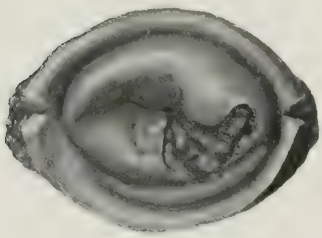

FIG. 7.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting or Infiltration (Gyn. Path. No. ——).

Patient 49 years old; 3 children (youngest 21); menopause one and a half years ago. No bleeding, but a profuse discharge requiring the use of a douche had been present for nine months and six months ago her physician recognized "an ulcer" on the cervix, but did not suggest a diagnosis of cancer until two weeks before operation. Pain in the left side (due to metastases) was very severe. General condition was only fairly good.

Uterus was freely movable and parametrium was apparently normal. Vaginal portion of the cervix (natural size and not curetted), shows a superficial ulcer situated in the outer half of posterior lip, edges undermined, and base firm, did not bleed on palpation. Tissue just about the ulcer was indurated.

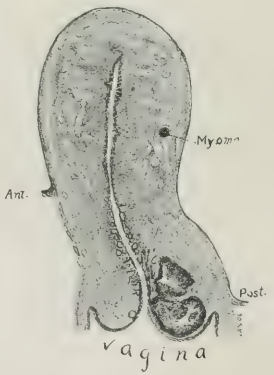

FIG. 8.—Stained Sagittal Section of the Uterus (slightly reduced) shown in Fig. 7.

A small primary growth is situated in the tissue of the posterior wall of the cervix (section is taken just mesial to the ulcer in the cervix). This section shows a characteristic feature of this type of growth and that is it extends by the invasion of the deeper cervical tissues and not by spreading, over the surface; also seen in the preceding case.

Cancer was not found in the parametrium, but the pelvic lymph nodes of the left side of the pelvis were extensively diseased.

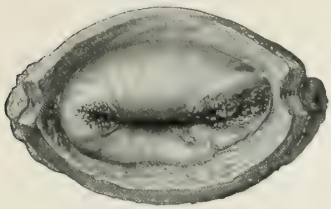

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FIG. 9.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting, Possibly a Double Focus (Gyn. Path. No. 6848).

Patient 58 years old; 13 children (30-9 years); menopause two and a half years ago. Only symptom had been a slight but constant blood-tinged discharge of eight months' duration following a slight hæmorrhage at the onset. Condition was good, hæmoglobin 90 per cent.

Uterus was freely movable and parametrium was apparently normal.

Vaginal portion of the cervix (natural size and not curetted) shows two small superficial ulcers, situated in each corner of the external os and spreading over the outer surface of the cervix. The bases of these ulcers are covered by friable tissue which bled easily on palpation.

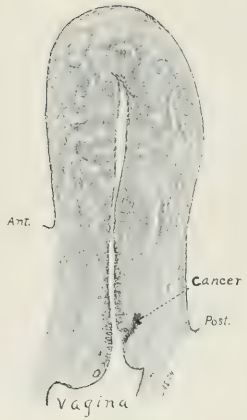

FIG. 10.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 9.

A small cancerous area is present in the posterior lip which as an "isthmus" unites the two areas of cancerous tissue situated on each side. Cancer was not found in either the parametrium or pelvic lymph nodes.

A very early case, but clinically of eight months' duration.

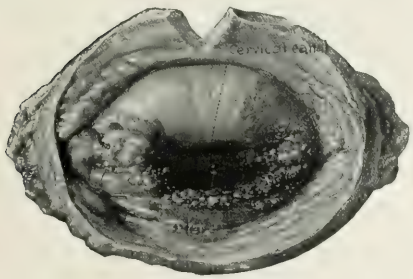

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FIG. 11.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting; Extensive (Gyn. Path. No. 7077).

Patient 36 years old; 1 child (age ?). History was unsatisfactory. Bleeding had been present for only a few days, but probably the patient had been curetted a month before her admission. Pain, of seven weeks' duration, was probably due to the extensive pelvic inflammatory disease which was present. General condition was excellent, hæmoglobin 100 per cent.

Movements of the uterus were restricted by pelvic adhesions. Parametrium on left side felt slightly indurated.

Vaginal portion of the cervix (natural size, curetted ? a month ago) shows a necrotic ulcer involving the entire posterior lip and the outer portions of the anterior, which bled easily on palpation.

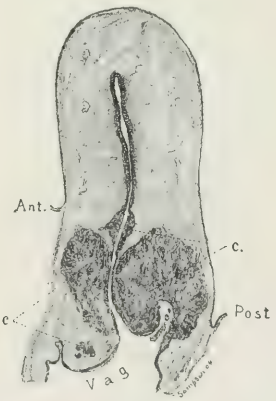

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FIG. 12. Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 11.

The growth has invaded the tissues of the cervix and has surrounded the cervical canal, in places involving it. The growth stops at the internal os.

The parametrium of the left side was invaded by direct extension and that of the right by metastases. Metastases were also found in the pelvic lymph nodes of the left side.

An extensive growth with a clinical history of short duration.

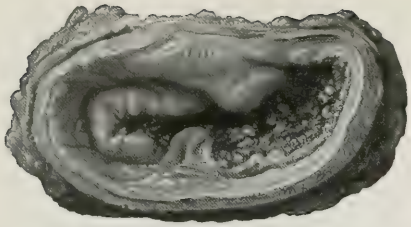

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FIG. 13.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting, with Extensive Necrosis (Gyn. Path. No. 7602).

Patient 40 years old; 3 children (age ?). Uterine bleeding and a foul discharge had been present for eight months, patient had been treated locally with electricity, twice a week, during the last four months. Pain, she had, was probably due to the pelvic inflammatory disease. General condition was fairly good, hæmoglobin 70 per cent.

Movements of the uterus were slightly restricted and the involvement of the left side of the vagina probably accounted for the apparent indurated parametrium of that side.

Vaginal portion of the cervix (natural size and never curetted), shows that the cervix has been converted into a craterous cavity lined by friable cancerous tissue, which has destroyed the greater portion of the vaginal portion of the cervix and has invaded the left side of the vagina.

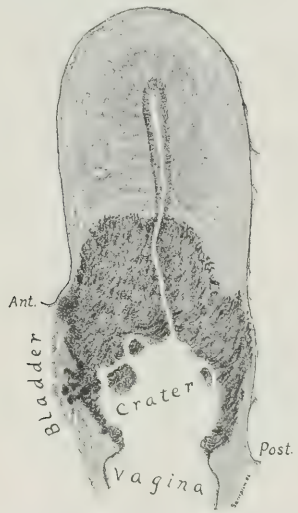

FIG. 15.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting; Extension with Involvement of the Bladder (Gyn. Path. No. 6715).

Patient 36 years old; 7 children (18-5 years). Uterine bleeding, alternating with a foul discharge, had been present for four months. Slight pain in the lower abdomen was probably due to adhesions from the pelvic inflammatory disease. General condition was fairly good.

Movements of the uterus were limited by the pelvic inflammatory disease and extension of the disease into the parametrium.

Stained sagittal section of the uterus demonstrates the invasion of the bladder muscle and the craterous cavity resulting from the necrosis of the cancer. The disease had invaded both parametria and had metastasized to the pelvic lymph nodes. The body of the uterus is beginning to be invaded by the growth.

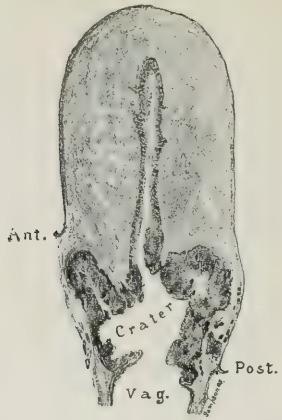

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FIG. 14.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 13.

The cavity was caused by the necrosis of the cancer and shows how the disease usually stops at the level of the internal os.

Parametrium of both sides were involved by a direct extension of the disease and a metastasis to a parametrial lymph node was found in the left side. Cancer was not found in the pelvic lymph nodes examined.

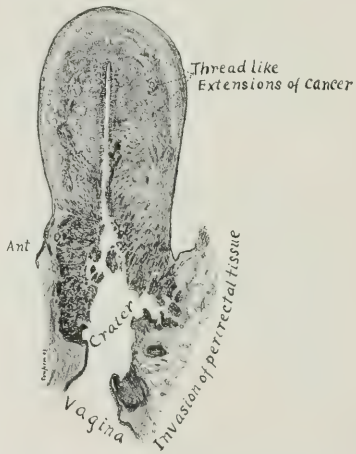

FIG. 16.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting; Extension with Obliteration of the Cul-de-sac and beginning Involvement of the Rectum (Gyn. Path. No. 7419).

Patient 37 years old; 6 children (14 years to 13 months). Bleeding, of ten months' duration, began three months after her last pregnancy. Condition was fairly good, hæmoglobin 73 per cent.

Movements of the uterus were restricted by the extension of the growth posteriorly and also by the apparent induration of the parametrium.

Stained sagittal section of the uterus shows the craterous cavity resulting from the necrosis of the growth, the extension of the disease into the body of the uterus as thread-like processes and the direct extension of the disease posteriorly obliterating the cul-de-sac and invading the tissue about the rectum.

The parametrium was involved by direct extension and cancer had metastasized to the pelvic lymph nodes.

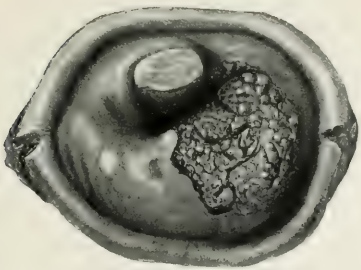

FIG. 17.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; both Inverting and Everting (Gyn. Path. No. 7467).

Patient 50 years old; 3 children (25-20 years); menopause one year ago. Bleeding had been present for three months, first noticed when straining at stool, severe hæmorrhages six weeks ago, and more or less constant offensive watery discharge, but no pain. General condition was good, hæmoglobin 74 per cent.

Movements of uterus were limited by pelvic adhesions, but the parametrium felt normal.

Vaginal portion of the cervix (natural size and not curetted), shows that the entire cervix is indurated and the outer portion of the posterior lip has become "ulcerated" and from the floor of the ulcer has arisen a cauliflower or everting growth. Another cauliflower growth is seen, about to "burst through" the center of the anterior lip.

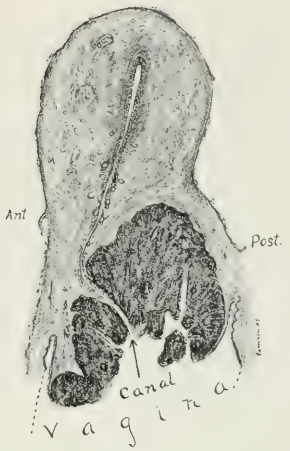

FIG. 18.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 17.

The growth is invading the cervical tissue *en masse* and in the posterior wall has reached the level of the internal cervical os. Notice how it grows through the cervical tissue and not along the cervical canal.

The adhesions on the surface of the uterus are shown. Cancer was not found in either the parametrium or pelvic lymph nodes removed.

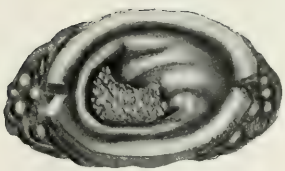

FIG. 19.—Squamous Cell Carcinoma, Cervical Canal; Everting, Causing Occlusion of the Canal and Pyometra (Gyn Path. No. 7658).

Patient 63 years old; 7 children (youngest 26); menopause sixteen years ago. Bleeding for three months had been the only symptom. General condition was excellent, hæmoglobin 85 per cent.

Movements of the uterus were limited by pelvic adhesions from double pyosalpinx, probably secondary to pyometra. Parametrium on both sides was indurated.

Vaginal portion of the cervix (natural size and not curetted) has become indurated, retracted and puckered and protruding from the external os is a cauliflower or everting growth.

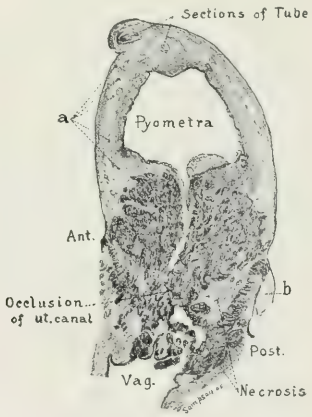

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FIG. 20.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 19.

The canal has been occluded by the growth, causing a pyometra. The fundus has become invaded by thread-like extensions of the growth (a) and the invasion of an adherent epiploical appendage of the sigmoid (b) is shown. The retracted shrunken and puckered vaginal portion of the cervix is also shown.

The parametrium on both sides was invaded by the growth and metastases to the pelvic lymph nodes were found.

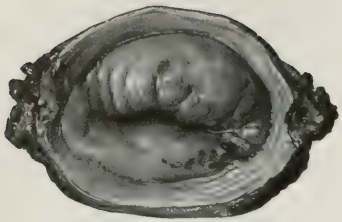

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FIG. 21.—Squamous Cell Carcinoma, Cervical Canal; Inverting (Gyn. Path. No. 8153).

Patient 46 ? years old; 9 children (youngest 10 years). History very unsatisfactory, but symptoms apparently of very short duration. Diagnosis was made by curetting a small piece of tissue from within the external os. General condition was excellent.

Uterus was freely movable and parametrium on both sides was apparently normal.

Vaginal portion of the cervix (natural size, had been curetted) showed absence of vaginal epithelium about the external os, probably caused by the curette. The anterior lip was a little retracted about the external os and just within the canal could be seen friable cancerous tissue.

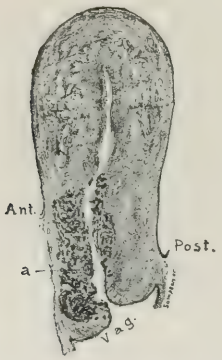

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FIG. 22.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 21.

The growth has started within the canal and has involved the latter as high as the internal os and is invading the cervical tissue on all sides in a diffuse manner. (a) represents the junction of the vaginal mucosa and the growth within the posterior lip.

Cancer was not found in the parametrium. The pelvic lymph nodes had not been removed.

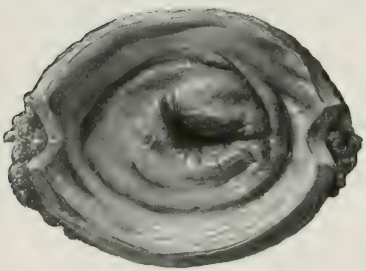

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FIG. 23.—Squamous Cell Carcinoma, Cervical Canal; Inverting. A Later Stage than One Shown in Fig. 21 (Gyn. Path. No. 6074).

Patient 54 years old; 6 children (youngest age ?); menopause eight years ago. Bleeding had been present for eight months, constant but never profuse; no other symptoms. General condition was good, hæmoglobin 75 per cent.

Uterus was movable, parametrium of the right side was apparently normal, that of the left side felt slightly indurated.

Vaginal portion of the cervix (natural size—small piece removed from within the canal for diagnosis) shows very well the indurated, retracted, and puckered vaginal portion of the cervix caused by the invasion of the cervical tissues from above.

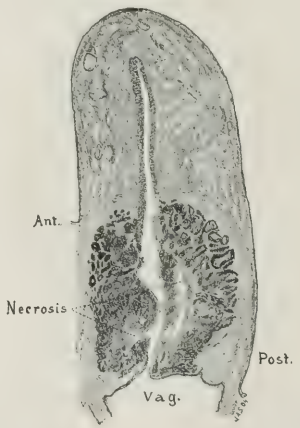

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FIG. 24.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 23.

The growth has started within the canal and has involved nearly the entire cervix extending above as high as the internal os. Metastases had occurred to the lymph nodes of both the parametrium and the sides of the pelvis.

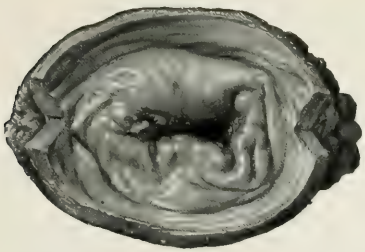

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FIG. 25.—Squamous Cell Carcinoma, Cervical Canal; Inverting. A later stage than the one shown in Figs. 23 and 24 (Gyn. Path. No. 6860).

Patient 48 years old; 8 children (aged ?); still menstruating. Bleeding had been of eighteen months' duration, foul watery discharge of shorter duration, some pain possibly due to the adhesions from a previous pelvic inflammation. Uterine polyp, may have accounted for some of the bleeding. Condition was fairly good, hæmoglobin 80 per cent.

Movements of the uterus were restricted and parametria of both sides felt indurated.

Vaginal portion of the cervix (natural size and never curetted) shows very well how the growth within may be very extensive and yet the vaginal portion of the cervix may be but very little involved. Notice the shrunken, puckered, and retracted vaginal portion of the cervix caused by the necrosis of the growth.

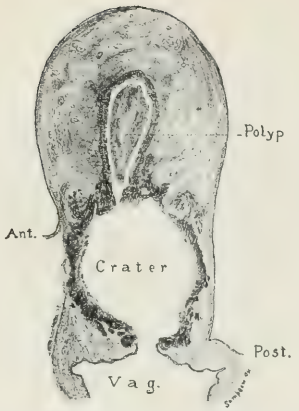

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FIG. 26.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 25.

The "craterous" cavity resulting from the necrosis of the growth is shown and the latter is beginning to invade the body of the uterus. A polyp is present in the fundus.

There was hypertrophy of the connective tissue of the parametrium, but the primary growth was apparently limited to the uterus. Metastases were found in the pelvic lymph nodes of both sides.

FIG. 27.—Squamous Cell Carcinoma, Cervical Canal; Inverting. An Extensive Growth of "Scirrhus" type (Gyn. Path. No. 7468).

Patient 37 year old; 7 children (15-2½ years). Bleeding had been the only symptom; of two years' duration, at first irregular but very profuse; constant the last three months. Patient was anæmic, hæmoglobin 55 per cent.

Parametrium was apparently indurated, growth had involved the deeper tissues of the vagina, all around the cervix.

Vaginal portion of the cervix (natural size, never curetted), shows that both lips present an "eroded" appearance with an irregular "fringe" of vaginal mucosa about the circumference. The eroded portion of the cervix appears "honey-combed" and the vagina about the cervix is indurated as a result of the invasion of its deeper tissues.

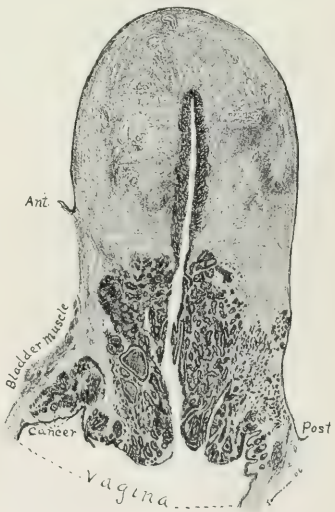

FIG. 28.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 27.

The growth is shown invading the deeper vaginal tissue, and the vaginal mucosa of the vaginal portion has sloughed off from the greater portion of both cervical lips. The disease does not extend above the internal os.

The growth had also extended in the parametrium of both sides, but cancer was not found in the pelvic lymph nodes removed,

FIG. 29.—Squamous Cell Carcinoma; Inverting; Origin ? but probably Vaginal Portion of Cervix (Gyn. Path. No. 7370).

Patient 35 years old; 2 children (ages?). A leucorrhœal discharge had been present for six months, bloody every time she had sexual intercourse or used a douche. Pain, for several years, was due to pelvic adhesions from previous inflammatory trouble. General condition was fair, hæmoglobin 75 per cent.

Uterus was adherent, parametrium on both sides indurated, and posterior vaginal wall involved.

Vaginal portion of the cervix (natural size, never curetted), shows that both lips present an "eroded" appearance, the posterior lip being much larger than the anterior, and on the outer right half of the latter a small area of mucosa is still present. The growth has involved the entire posterior vaginal wall, causing a large ulcer whose floor is composed of friable cancerous tissue.

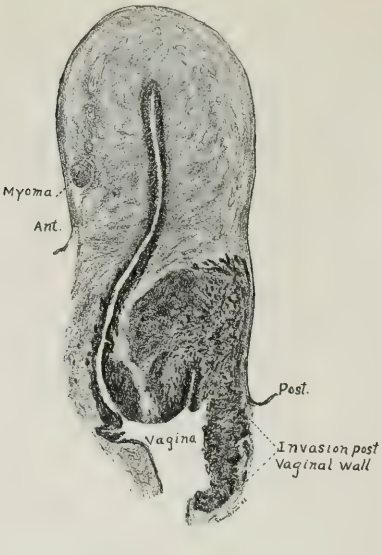

FIG. 30.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 29.

The growth is limited almost entirely to the deeper tissues of the posterior cervical wall and vagina. The cervical canal is involved only about the external os and for a short distance within, the anterior lip is compressed, and involved only about the external os.

Cancer was found in both the parametrium and pelvic lymph nodes.

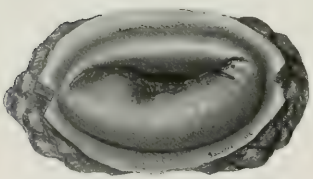

FIG. 31.—Adenocarcinoma; Cervical Canal—Originally Everting (Gyn. Path. 6603).

Patient 37 years old; 4 children (21-15 years). Bleeding began seventeen months ago, and seven months ago a fungoid growth was removed from the cervix and there has not been any bleeding since, but for the last five months there has been severe pain in lower abdomen and back, requiring morphia. General condition was fairly good, hæmoglobin 60 per cent.

Uterus was movable, parametrium of each side felt normal.

Vaginal portion of the cervix (natural size and from which a fungoid growth had been removed seven months ago) shows that both cervical lips appear normal, but the external os is a little enlarged, edges ragged, and within can be seen and felt friable tissue.

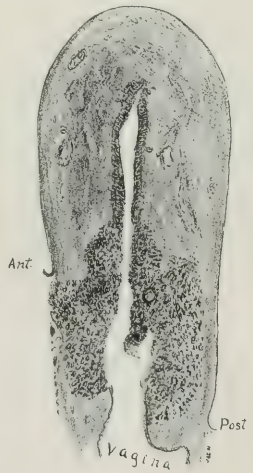

FIG. 32.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 31.

An adenomatous growth has invaded nearly the entire cervix about the external os and is gradually replacing the endometrium of the body of the uterus.

Cancer was present in both the parametrium and pelvic lymph nodes.

FIG. 33.—Adeno-carcinoma, Probably Starting in the Cervical Canal; Inverting (J. H. H., Path. No. 2377).

Patient 40 years old; 7 children (13-2 years). Bleeding for six months had been the only symptom. Local treatment before entering the hospital (length of time?). General condition was bad.

Uterus was movable, some induration of the left parametrium. Patient died from cerebral embolism, following acute endocarditis. Specimen was obtained at autopsy a few hours after death.

Vaginal portion of the cervix (natural size, local treatment, including curettage for sometime before patient came to hospital), shows that about one-third of the surface is covered by mucosa, while the rest presents an "eroded" appearance, the extreme left side and also the portion of the anterior lip about the external os being composed of friable tissue which bled on palpation. A small cancerous nodule was found in the anterior vaginal wall about 1.5 cm. from the cervix.

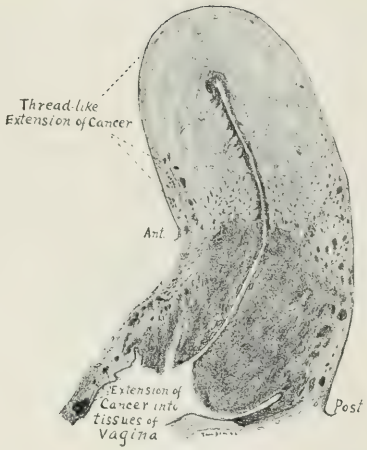

FIG. 34.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 33.

The growth apparently started from the deep cervical glands, the superficial cervical mucosa being for the most part intact. The growth has invaded the body of the uterus and the deep tissues of the vagina.

Cancer was found in the parametrium of both sides, liver, diaphragm, lungs and thoracic, abdominal and pelvic lymphatics.

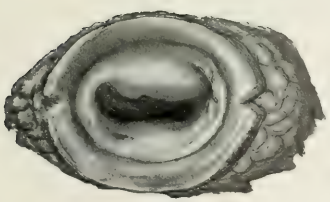

FIG. 35.—Adeno-carcinoma; Cervical Canal, with Possibly Squamous Cell Carcinoma of Vaginal Portion of Cervix (Gyn. Path. No. 8154).

Patient 62 years old; 4 children (41-35 years); menopause seventeen years ago. Constant bloody discharge had been present for seven months, and at times bearing-down pains in the uterus. Condition was fairly good.

Movements of the uterus were restricted by adhesions from previous pelvic inflammation. Parametrium on the left side felt indurated.

Vaginal portion of the cervix (natural size and never curetted) shows the shrunken, puckered, and retracted cervix, so characteristic of the advanced cases of cancer developing within the canal. Just within the external os, friable tissue which bled easily could be palpated.

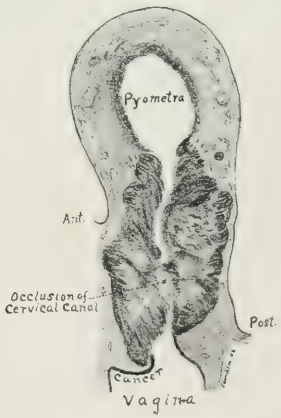

FIG. 36.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 35.

The growth has occluded the cervical canal causing pyometra. It is also beginning to invade the body of the uterus. The vaginal portion of the uterus is apparently covered by a thin layer of cancerous tissue of the squamous cell type which, to the naked eye, looks like the normal mucosa.

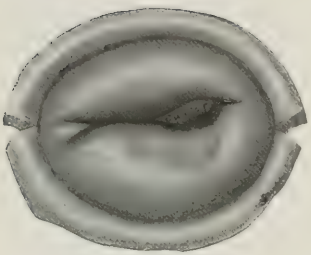

FIG. 37.—Adeno-carcinoma ?; Cervical Canal; Inverting. Very Malignant (Gyn. Path. No. 6763).

Patient 41 years old; 1 child (9 years). Only symptom was bleeding, of three weeks' duration. General condition was excellent, hæmoglobin 85 per cent.

Uterus was freely movable; apparently a very early growth.

Vaginal portion of the cervix (natural size, a small piece had been removed from within the external os for diagnosis) is apparently normal for a parous woman, except for a small nodule of tissue seen just within the external os and apparently arising from the anterior cervical wall.

FIG. 38.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 37.

A growth has arisen from within the cervical canal, apparently an adenocarcinoma. It has spread over the posterior surface of the cervical canal and is invading the deeper tissues. The anterior surface of the canal is involved just within the external os; a second cancerous nodule or part of the primary growth is seen just posterior to the other. It was impossible to determine its exact relation to the first one. Cancer was not found in the parametrium. The growth recurred soon after operation.

the fifteen cases, there was a history of neglected uterine bleeding for six months or more, but in two cases with metastases to the pelvic lymph nodes this was of less than two months' duration. As the disease invades the cervical tissue, necrosis usually occurs with a resulting ulcer. Occasionally the tumor may increase greatly in size with but very little necrosis, but usually the one closely follows the other. As the cervical tissue becomes invaded by the growth necrosis usually occurs, later the cervical canal becomes surrounded, then invaded and the central core of the cervix may slough away, and thus convert the cervix into a crater lined with cancerous tissue.

In the seven cases of bleeding for six months or over, the cervix had been converted into a crater in four of the cases. While a long duration usually indicates an extensive growth it does not necessarily follow as shown in Fig. 9, nor does one of apparently short duration indicate an early one, see Fig. 11.

This type of growth is a very unfavorable one, usually soon invading the surrounding tissues and even metastasizing before the latter becomes involved. The symptoms may appear early or late, depending on how soon necrosis appears and its extent. We are unable to make a definite prognosis from the history of the case, or the results of clinical or pathological examinations unless it be that if metastases are present the prognosis is very unfavorable. A history of long duration may reveal an early growth, one of short duration an extensive one, and a small primary growth may give rise to metastases and an extensive one may still be local.

Squamous Cell Carcinoma—Cervical Canal.

This occurred in five instances, in four cases inverting and in one everting. In the latter case, pyometra was present. The inverting type of growth undergoes the same changes as the inverting type arising from the vaginal portion of the cervix. It, however, offers the additional clinical disadvantage that it is situated within the cervical canal and this renders its diagnosis by inspection or palpation more difficult. It is remarkable how far advanced the growth may be and yet the mucosa of the vaginal portion of the cervix may be intact or but little involved, as shown in the illustrations. There is one very important clinical feature to be emphasized and that is the induration, retraction, and puckering of the vaginal portion of the cervix caused by the growth invading it from above, analagous to a similar condition of the skin or nipple of the breast usually seen in cancer of that organ.

The Clinical Significance of Adeno-carcinoma of the Cervix.

There were but four instances of this type of growth, and all arose in the cervical canal. One was probably of the everting type but the everting part had been removed before I saw the patient. In all specimens the growth had extended beyond the uterus, and all four patients are dead. One died from cerebral embolism due to acute endocarditis, another died on the fifteenth day after hysterectomy, and the two others died from recurrences within a year and a half after hysterectomy. All four cases could not have been cured at the time of the operation. Bleeding as a symptom was present in these four cases; in one three weeks, in the three others six, seven, and seventeen months, respectively.

These four cases support the view that this is the most malignant form of uterine cancer.

CONCLUSIONS.

From a study of these cases, some of the types of cervical cancer may be seen and the changes they undergo as the disease progresses, and from this study we are able to understand the clinical manifestations of the disease. One very important feature must be emphasized and that is the importance of an early diagnosis, for the parametrium was involved in seventeen of the twenty-seven operable cases and the pelvic lymph nodes were involved in nine out of nineteen cases where they were removed and studied. In three of the nine cases in which the pelvic lymph nodes were involved, the parametrium was free, thus demonstrating that, in at least twenty of the twenty-seven cases, the growth had extended beyond the uterus.

One hopeful sign, however, was present and that is there was a history of neglected uterine bleeding for six months or more in over half of the cases. Put back the growth where it was six or even two months before the cases were operated upon and probably it would have been local in the majority of them. What we need is a *prophylaxis* of the incurable stage, and that can come only by the education of both physician and patient, the former first; and to him this contribution is offered.

STUDIES IN GENITO-URINARY SURGERY

THE JOHNS HOPKINS HOSPITAL REPORTS, Volumes XIII and XIV, will be issued in January, 1907. Volume XIII will consist of about 605 pages with 201 figures in the text, six plates and one colored chart.

Volume XIV will consist of about 632 pages, and have 97 figures in the text.

The price of each volume will be five dollars ($5.00), bound in paper, and five dollars and fifty cents ($5.50), bound in cloth.

Remittances and orders will now be received.

THE JOHNS HOPKINS PRESS, BALTIMORE, MD.

THE SURGERY OF BLOOD VESSELS, ETC.[1]

By Alexis Carrel.

Vascular surgery may be considered from the standpoint of the treatment of lesions of blood vessels proper, and from the standpoint of general therapeutics of tissues and organs. Treatment of lesions of the blood vessels, such as wounds, aneurisms, varices, etc., constitutes classical vascular surgery, and its discussion therefore is unnecessary. Application of the vascular operations to general surgery is an almost unexplored field. I shall discuss to-night a few experiments of this character that Dr. Guthrie and I have performed since last August. I began these researches in 1901-1902 at the University of Lyons, and continued them last year with Dr. Guthrie at the University of Chicago, through the kindness of Dr. Stewart, who granted us the facilities of his laboratory.

I shall describe, first, *the operative methods,* second, their *experimental applications,* and third their *hypothetical applications to human therapeutics.*

A. Methods.

We use operations acting directly on blood vessels and operations acting indirectly on blood vessels through their nerves.

I. Operations acting directly on Blood Vessels are Five in Number: Partial Stenosis, Longitudinal Exclusion, Patching, Anastomoses, and Transplantations of Arteries and Veins.

In performing these operations certain general rules must be observed. It is known that failure in vascular surgery is mainly due to the formation of a thrombus. Pathological physiology of blood vessels shows that thrombosis may be caused by an inflammation of the endothelium, by a wound, even such as a slight crushing of the endothelium, by a lack of continuity of the intimal layers of the vessels, or by the presence of some foreign tissues or juices in the lumen of the vessel. Each detail of the technique (1), therefore, has been developed and adopted with the view of eliminating these sources of complication.

A rigid *asepsis* is absolutely essential for success. It seems that the degree of asepsis under which general surgical operations can successfully be performed may be insufficient for good results in vascular operations. Generally, it is considered that a wound is aseptic when it does not suppurate, and when healing occurs "per primam intentionem." But it should be remembered that this clinical asepsis is far from the ideal condition of absolute asepsis. Between absolute asepsis and infection, which is evidenced by the ordinary symptoms of inflammation, there are many intermediate degrees of attenuated infection. It is certain that every surgical wound, though clinically aseptic, is more or less infected. This infection may not be accompanied by the classical symptoms of inflammation; or if these phenomena are present, they may escape detection. The tissues unite "per primam intentionem," and from a clinical standpoint all the reparative processes occur as if the wound were really aseptic. But it is very probable that the more marked degree of these slight infections may be sufficient to cause thrombosis and that in order to obtain constant good results in blood vessel surgery the degree of asepsis must be higher than in general surgery.

The *dissection* of the vessel is not dangerous if the wall of the vessel is not crushed or roughly handled with metallic forceps or other hard instruments. Even the veins may be closely dissected and freely handled with the fingers without being injured, provided the wall be not hurt by a sharp instrument.

When *temporary hemostasis* is obtained by means of forceps or clamps, the endothelium is often wounded, and coagulation occurs at the injured point. It is necessary that these clamps be smooth-jawed and not too strong in the spring. We have abandoned completely this method of temporary hemostasis. The circulation is stopped by a narrow linen strip which is placed around the vessel, and then drawn tight and fixed by a serre-fine. This method does not injure the wall of the vessel and its application is almost as rapid and no more difficult than the application of ordinary forceps. This small detail is of very great importance for successful results.

After section of the vessel, the *external sheath is resected* or *removed* from the edges of the lumen. For if it get between the edges of the vessels, which is very liable to happen, and come in contact with the blood, it very quickly leads to the formation of a thrombus. Next the lumen of the vessel is carefully washed with isotonic sodium chloride solution (0.9 per cent) and as a rule coated with vaseline. The vessel can be handled with very delicate forceps, if care is taken to grasp only the extreme edge of the wall.

On large arteries it is possible to make the suture by interstitial stitches without injuring the endothelium. But it is impossible on veins and on medium-sized and small arteries. As a rule perforating stitches are used, which, of course, produce wounds through the endothelium. Consequently it is necessary to render these wounds as harmless as possible. By using very sharp, round needles (No. 15 or 16), only extremely small wounds are made. As the vessel wall is very elastic and as it is stretched when the needle punctures it, the result is that it contracts down and holds the thread firmly. The threads are sterilized in vaseline and are kept heavily coated with it while suturing. The vaseline is rubbed off in the holes and prevents the wounded tissues and the blood from coming into actual contact.

Great care is taken not to include fragments of the connective tissue layer in the line of suturing, and to obtain a smooth union and approximation of the endothelial coats.

[1] Read before the Johns Hopkins Hospital Medical Society, April 23, 1906.

When these general rules are observed, the following operations are practically always successful.

1. *Partial stenosis.*—It consists of diminishing the size of the lumen of a vessel by one or more perforating stitches. The vessel is flattened between the fingers and transfixed with a fine needle in such a manner that the lumen is reduced as much as desired. The ligature is then drawn through and the two ends tied about the portion it is desired to occlude. A small hemorrhage occurs along the thread when it is drawn through, but this stops when the thread is tied.

This operation has been performed on the aorta, the carotid artery, and the portal vein of dogs, with the view of diminishing the circulation in the peripheral portions of the vessels (as Dr. Halsted (2) has done by the use of silver bands around the vessel). It was used also to increase the pressure of the portal vein and force its blood through the kidney, the renal artery being anastomosed with the splenic vein. It will be of value in producing congestion of an organ by diminishing the caliber of the veins in cases where this condition is desired.

2. *Longitudinal exclusion.*—It consists in isolating from the blood current a portion of the vessel of some length. Without interrupting the circulation continuous mattress sutures are made in such a manner that a longitudinal segment of the vessel is closed. This operation has been performed on the aorta and on the carotid. It is somewhat analogous to the reconstruction of the aorta proposed by Matas (3).

3. *Patching.*—This consists in closing an opening made through the wall of a vessel by sewing in it a portion of the wall of another vessel. For instance, an opening is made through the anterior wall of the carotid artery. A flap of proper size is resected from the wall of the external jugular vein. The edges of the venous flap are sutured to the edges of the arterial opening, and the circulation is re-established. It is possible to use a flap of peritoneum instead of a flap of vein. Three months ago, a small portion of the abdominal aorta of a cat having been extirpated, the wound was closed by a flap of peritoneum. Immediately after the circulation was re-established, the pulsations of the femoral arteries were normal and have remained so to the present time. The primary aim of the patching was the reparation of a vascular lesion, but it was also a preliminary step in the development of a method of lateral implantation of very small vessels. For instance, the spermatic artery of a medium-sized dog (20 K.) is so small that direct anastomosis is not feasible; but by dissecting it as far as the aorta and cutting out a triangular aortic flap, in the center of which is the mouth of the spermatic artery, and then suturing this flap on to a proper opening of the femoral or carotid arteries of another dog, successful transplantation may be performed. By this method, it is possible to transplant the smallest vessels.

4. *The direct vascular anastomoses* are made by uniting the edges of the openings of the vessels by a continuous suture (4 and 1). The *termino-terminal, latero-terminal* and *latero-lateral varieties* have been successfully established by this method with little difficulty.

The *termino-terminal anastomosis* is probably the most valuable. The most important stage of the operation is the approximation of the ends of the vessels by three threads applied in three equidistant points of the circumference of the vessels. Traction on each thread transforms the circumference into a triangle. While the sides of the triangle are stretched a continuous suture is made along each of them. The end to end suturing of the carotid artery of a dog can be performed in four or five minutes.

In the *termino-lateral anastomosis,* the end of the smaller vessel is united to a triangular opening made through the wall of the larger one.

The *latero-lateral anastomosis* consists simply of uniting by continuous suture and two triangular or ellipsoidal openings made through the wall of the vessels. This variety is used in our new method of making Eck's fistula.

This technique has some important modifications in the *arterio-arterial, veno-venous and arterio-venous varieties* (5), but the general principle is the same.

The main complications are hemorrhage, stenosis, and thrombosis. Hemorrhage occurs sometimes in arterio-venous anastomosis immediately after the re-establishment of the circulation. It is easily controlled by one or two additional stitches. Stenosis is very seldom observed; it never occurs when the edges are properly approximated and stretched during the suturing. Thrombosis is produced by infection or some grave fault of technique. For instance, in a case of transplantation of the kidneys in a cat, paralysis of the posterior limbs occurred a few hours after the operation. Post-mortem examination showed a complete obliteration of the lower aortic anastomosis, due to a lack of suturing of one-third of the circumference of the artery. The external sheath only was sutured, and of course, coagulation of the blood occurred.

Such complications are exceptional, and practically always the results are good, even after a long time. Clinical and anatomical examinations made six months-and-a-half to nine months after the operation demonstrated that the circulation through the anastomoses was as active as on the day of the operation, and that the anastomoses were perfectly sound and covered with a glistening and apparently normal endothelium.

5. *The transplantations of arteries and veins* (6).—There are two kinds of transplantations of arteries and veins, uniterminal and biterminal.

The *uniterminal transplantation* consists in grafting one end of a divided vessel into another point of the circulatory apparatus (7). There are many varieties of this kind of transplantation according to the nature of the vessels and to the combinations of their ends. An artery can be transplanted on a vein or another artery. A vein can be transplanted on an artery or another vein. On the other hand, the central or the peripheral end of a vessel can be transplanted on the central or peripheral end of another vessel or on its lateral wall. I have not time, of course, to describe each one of these varieties.

The main result of the uniterminal transplantation is to change the nature of the circulating blood, and to modify its

pressure. For instance, when the peripheral end of the external jugular vein is anastomosed with the central end of the carotid artery, the vein becomes filled with red blood; its pressure is increased while the pressure of the artery is diminished. From an anatomical standpoint, the vessels adapt themselves very quickly to these modifications of blood pressure. When the normal pressure of the carotid artery is increased by directing all its blood into a closed venous system, like the inferior thyroid vein, the wall of this artery becomes thicker. After a few months there is a hypertrophy of the muscular coat, and of the intima, changes which are similar to the internal and medial varieties of arterio sclerosis in man (8). It shows that in some cases arterio-sclerosis may be produced by a mere increase of blood pressure without intervention of toxic or microbian irritations. When the pressure of an artery is diminished by anastomosis with a large venous system, as the superficial veins of the neck, its wall undergoes phenomena of adaptation and becomes weaker. There is hypotrophy of the elastic and muscular elements of the middle coat. We intend, after having produced a sclerosis of the carotid, to try to cure it in producing a constant lowering of the blood pressure by a proper anastomosis.

When a circulation of red blood is established through a vein (9), its wall reacts very quickly by thickening itself. This thickening is produced mainly by the increase of blood pressure. The degree of thickening of the wall depends on the degree of the increase of blood pressure. When the vein supports a high pressure but lower than the normal arterial blood pressure, its wall becomes considerably thicker, its lumen is dilated and the circulation even after nine months is extremely active. It seems that the process of reaction stops when the thickening has reached a certain degree. On the contrary, when the venous wall has to support the normal arterial pressure, the thickening is very great. It seems that the process of reaction does not stop and may ultimately lead to a complete obliteration of the vein. After six months and a half, there was little circulation through the peripheral branches of a thyroid vein, which was anastomosed end-to-end to the carotid artery. All the blood of the carotid artery had been forced into the thyroid veins, and under this pressure, the wall had reacted as evidenced by extensive sclerosis.

The biterminal transplantation consists of cutting out a segment of a vessel and of interposing this segment between the cut ends of another vessel. It is termed *incomplete* when the vascular segment is allowed to retain its collaterals and its normal relations with the surrounding tissues. For instance, the ends of a segment of the femoral vein are cut, and anastomosed to the corresponding cut ends of the femoral artery. It is termed *complete* when a venous segment is completely extirpated and interposed between the cut ends of another vessel. An arterial or venous segment extirpated from an animal may be transplanted on the same animal or another animal. For instance, a venous segment is resected from a dog and substituted for a portion of the carotid artery of the same dog. It is an autoplastic transplantation. Homoplastic transplantations have also been performed. For instance, a segment of the aorta or the vena cava is extirpated and interposed between the cut ends of the aorta or vena cava of another animal.

After transplantation the nutrition of the vascular wall is excellent, the cicatrization of the ends is quickly made, and the circulation is perfect. The interruption of the circulation, which lasts from 20 minutes to two hours, does not appear to interfere with the nutrition of the vascular wall, and by taking care to preserve the vessel in sodium chloride or other suitable solution, it seems probable that the circulation could be interrupted longer without danger. When venous or arterial segments are transplanted respectively on a vein or an artery, no apparent changes in their structure occur. But when a venous segment is transplanted on an artery, it rapidly undergoes very pronounced modifications. There is no dilatation of the lumen of the vein. On the contrary, the venous wall reacts against the arterial blood pressure and becomes thickened. Fourteen days after the operation the venous wall was found very much thicker than the wall of the artery (10). This thickening was due mainly to hyperproduction of connective tissue, and to hypertrophy of the muscular and elastic portions of the venous wall. We do not yet know whether this thickening progresses indefinitely and leads to stenosis or obliteration of the vessels. Five months after the operation a venous segment transplanted on the carotid artery exhibits the appearance of an arterial segment, pulsates as an artery, and its circulation is very active.

We may conclude that the vessels adapt themselves very quickly to the changes of pressure and function. This power of adaptation makes vascular transplantations one of the fundamental operations of experimental blood vessel surgery.

II. Operations acting on the Blood Vessels through their Nerves.

Three kinds of operations have been performed: (11) *temporary partial or complete denervation* of the kidney, *elongation* and *crushing* of the nerves of the thyroid gland.

Temporary denervation consists of cutting the nerves of an organ and of anastomosing immediately the main fibres. For instance, the kidney of an animal is completely denervated by closely dissecting the vessels. Both ends of the main nerve may be anastomosed by using a fine needle. In one case the peripheral end was united to the great abdomino-genital nerve, in order to change the innervation.

Elongation and *crushing* of nerves are such simple operations that they do not need to be described.

It is well known that section of their nerves produces vasodilatation of organs. The physiological effects of denervation are easily observed after replantation and transplantation of organs. Complete denervation is not necessary, for a partial denervation of the kidney may be followed by marked vasodilator phenomena. Elongation and crushing produce effects similar to those produced by section of the nerves. This method of producing an increase of the circulation of organs must be considered as crude and inexact, as excitatory fibres as well as vaso-constrictor and vaso-dilator fibres are cut

at the same time. On the other hand, section of nerves is always more or less harmful. In order to develop a better method, it would be necessary to exactly establish the topography of the different kind of nerves. This might enable us to cut only the vaso-constrictor nerves. The ideal operation would be to produce a permanent excitation of the vaso-dilator or vaso-constrictor, or even excitator nerves, according to the needs of the organ. This question is now being studied, but the results as yet warrant no conclusions.

B. Experimental Applications.

The experimental applications of these operations are very numerous. It was quite impossible to make an exhaustive investigation of this large field within a few months with such facilities as we had. I shall briefly describe some experiments performed with the view of observing *the effects of artificial modifications* of the circulation *in the limbs, the head,* and *the organs;* and secondly, the *preliminary researches on the question of the transplantation of organs.*

I. Artificial Modifications of the Circulation in the Limbs, the Head, and the Organs.

We tried to *modify the circulation of the posterior limb* by lateral anastomosis of the femoral artery and vein and the cross end-to-end anastomosis of the femoral artery and vein, and the aorta and vena cava. The lateral arterio-venous anastomosis was proposed in 1902 by san Martin y Satrustigui as a treatment of gangrene (12). He established a lateral anastomosis between the femoral artery and vein on goats, but obliteration occurred. He also performed this operation on two patients affected with gangrene of the lower limb. In one case the operation was entirely unsuccessful, in the other the gangrene stopped, but this was probably due to the fact that the affected portion was amputated at the time the anastomosis was performed. Afterwards, Jabouley (13) made the same operation on a patient suffering from gangrene produced by endarteritis. The operation was not successful and amputation became necessary. The idea of san Martin y Satrustigui was ingenious but his method and also that of Jaboulay was wrong, because after a lateral arterio-venous anastomosis the larger part of the arterial blood instead of going towards the capillaries goes back towards the heart through the central end of the vein. At the same time the arterial blood pressure is considerably lowered. We have shown by performing on a dog a lateral anastomosis between the femoral artery and vein, that three hours after the operation the valves are still competent and that no red blood flows through the veins towards the capillaries, but that it flows towards the heart (14).

On the contrary, by performing a cross end-to-end anastomosis of the femoral artery and vein, the circulation is quickly reversed (14 and 15). An acute experiment on a dog showed that three hours after a termino-terminal anastomosis of the central end of the femoral artery to the peripheral end of the femoral vein, the veins of the thigh, the leg, and the foot were filled with red blood, and that the dark blood returned toward the heart through the arteries. Complete reversal of the circulation in the limb is practically achieved four hours after the operation. A dog with a partial reversion of the circulation in the posterior limb was kept alive for several weeks and no trouble occurred. But this does not prove that a complete reversal is not harmful for the nutrition of the limb. It is probable for many reasons that this operation will not have practical applications in the treatment of gangrene. It may, however, be useful for some other purposes. For instance, a preliminary study was made of a method for directing a current of red blood through the venous apparatus of the epiphysis of a bone, in order to increase the rate of its development. But at the present time no conclusion can be drawn as to whether or not this operation can give positive results. While a partial reversal of the circulation in a limb may be of value, a more extensive operation, as the simultaneous reversal of the circulation in both posterior limbs, is very dangerous. If, for instance, the central end of the abdominal aorta is united to the peripheral end of the vena cava and the central end of the vena cava to the peripheral end of the aorta, the circulation is immediately reversed in the lower part of the abdomen and the upper part of the hind limbs, the valves stopping the blood from the lower portion of the latter for a time. By degrees, however, they give way, and at the same time the animal may present symptoms of a very abundant hemorrhage, even becoming comatose. If at this stage the head be lowered and the posterior limb elevated, it immediately regains consciousness and shows ambulatory movements of the fore limbs. Post-mortem examination of such a case shows an enormous congestion of the veins below the level of anastomoses, the animal dying apparently by collection of the red blood in the venous system.

Artificial modifications of the circulation of the head and neck are easily obtained, for the veins are practically without valves.

The *transformation of the superficial veins of the neck into arteries* has often been performed by anastomosing the carotid and the external jugular vein. After several months all the superficial veins of the anterior part of the neck are still filled principally with red blood. Six months-and-a-half after the operation their walls were found to be markedly thickened. The subcutaneous veins were similar to small arteries, and the thickness of the skin was increased.

We tried to increase the circulation of the brain by directing a strong current of red blood through the internal jugular vein, the peripheral end of this vein being anastomosed to the central end of the common carotid artery. After this operation no clinical troubles occur in the dog, a dog operated on five months ago is living in good health, but it might not be the same in man, as in the latter the internal jugular vein is more important than in the former. This idea of using the veins to conduct the red blood to the brain is not a new one. Jaboulay in 1902 expressed the opinion that an arterio-venous anastomosis might have a good result in case of insufficient circulation, as in softening of the brain. I do not think that this kind of lesion can be successfully treated, but it is not

absolutely improbable that a slow and progressive disease such as cerebro-sclerosis might be benefited by an operation modifying the circulation. But on account of the special conditions of the circulation of the brain, the substitution of veins for arteries to advantage when the latter are rendered useless by some pathological processes, is doubtful.

A few operations were performed with the view of *regulating the arterial circulation of the brain* in such a way as to diminish the blood pressure or to protect the brain against sudden increase of the blood pressure.

We attempted to suppress the arterial pulsations in the upper part of the carotid artery. For this purpose the length of the carotid artery was increased and its shape modified by interposing between its cut ends a long and curved segment of vein. From a theoretical point of view the systolic wave should be altered by the difference in elasticity of this thin and half circular venous tube. The tracings taken above and below the venous segment showed that this view was true, as regards the immediate results. But these results cannot be permanent as the wall of the vein rapidly becomes greatly thickened. However, owing to its semicircular shape, the venous segment may alter the circulation in a manner similar to that effected by the normal curvature of the vertebral and the upper portion of the carotid artery.

We endeavored also to diminish the pressure of the cerebral arteries in order to modify their structure. The central end of the external jugular vein was implanted on the wall of the common carotid artery. A large part of the arterial blood flowed into the vein with a strong thrill. A tracing taken from the central end of the carotid of the other side showed a lowering of the pressure when the blood was allowed to escape into the vein. Still another and more radical operation was performed. The peripheral end of the carotid was united to the central end of the jugular vein, in such a manner that the circulation of the carotids were reversed. The carotid then became similar to a vein, only it carried red blood toward the heart. This anastomosis probably produces a lowering of the cerebral blood pressure. A sudden increase of the arterial pressure would probably produce less effect on the cerebral circulation than normally, owing to the escape of arterial blood into the venous system. This operation may protect the vessels of the brain against great actual variations of the blood pressure. A dog thus operated on eight months ago is still living and in good health, and will enable us to study the anatomical modifications of the vessels. It is not entirely unreasonable to believe that operations of this character may sometime be used to hinder cerebral hemorrhage and perhaps to treat sclerosis of the arteries by establishing a lower pressure in the cerebral vessels and so producing a modification of their anatomical structure. This is, of course, a mere hypothesis, and further experiments may show that it is quite impossible.

The artificial modifications of the circulation in organs may be accomplished in a number of different ways. A few of these possible operations have been performed with the intention of changing the kind of blood circulating through a gland. We have tried mainly to increase the amount of red blood, or, in other words, to produce arterial hyperemia of the organ.

The substitution of the blood of the portal vein for the red blood of the renal artery was made with the view of investigating whether an organ can live with only a circulation of dark blood. The peripheral end of the renal artery was anastomosed to the splenic vein, and the pressure artificially increased in the portal vein by producing a stenosis near the liver. The dark blood flowed through the renal artery, the kidney, the renal vein and into the vena cava. In one case the kidney was examined through an incision fifteen days after the operation. The renal tissue was very pale and soft, and on cutting it a hemorrhage of dark blood occurred. There was no secretion of urine. Also it would be very easy to make the venous blood from one kidney flow through the other kidney by anastomosing the peripheral end of the vein of the first kidney to the peripheral end of the artery of the second kidney. We intend also to suppress the red circulation of an exophthalmic goiter of a dog, and to supply the gland exclusively with dark blood.

Increase of the red blood supply of an organ has been secured by the complete reversal of the circulation, the transplantation of a large vein on an artery, and by temporary denervation or elongation of the nerves. Complete reversal of the circulation produced an arterial hyperæmia owing to the fact that the veins are larger than the corresponding arteries. It was tried on the kidney and successfully performed on a normal thyroid gland. The result was a temporary enlargement of the gland with increase of the circulation. The nutrition apparently remained unaltered. Transplantation of one or two large veins of the thyroid gland into the carotid artery produces a strong arterial hyperæmia. This hyperæmia is temporary for the venous wall reacts against the arterial blood pressure and becomes much thickened, the lumen being decreased in size so that several months after the operation the red circulation through the vein is greatly diminished. But even a temporary arterial hyperæmia produces great anatomical modifications in a pathological gland. This operation was performed four times on dogs presenting parenchymatous goiters. Although no conclusion can be drawn from these observations, one of them deserves description. An old dog had two very large parenchymatous goiters, which in shape, size, and consistency were similar. He presented some general symptoms attributable to an insufficient secretion of the thyroid gland. He was extremely fat, and had lost the hair from the lumbar and a part of the dorsal regions of his skin. He slept nearly all the time, or stupidly sat in a corner of the room. The operation was performed on the inferior thyroid vein of the right goiter, the left one being observed as a control. The vein became as large as the common carotid and exhibited the signs of having a strong arterial circulation. After a few days the right goiter began to decrease in size and became harder in consistency. At the same time the animal lost his excess of fat, hair grew rapidly on the bald spots, and he became very lively and pugnacious. Six months and a

half after the operation he was etherized and the goiter examined and extirpated. Profound modifications had occurred in the size and the consistency of the right goiter. It presented an appearance quite different from that of the left goiter. Its upper end, however, in which the circulation had not been modified showed a structure similar to that of the left side. Histological examination showed that the thyroid vesicles were very numerous, and the colloid substance abundant in the right gland, while very few were present in the left one. This shows that the increase of the red blood supply of a gland may perhaps produce modifications in its metabolism.

The circulation was increased in several cases by acting on the vaso motor nerves.

The operations of complete denervation, elongation and destruction of the nerves were performed on the normal thyroid gland. The results of these operations were a slight increase of the size of the organ and temporary exaggeration of the circulation. After a short time the gland regains its normal size. Temporary denervation was performed on the kidney. It produces at first the well-known effects of vaso dilatation and increase of the quantity of urine.

It is evident that there are other ways of modifying the circulation of an organ, and we have experiments planned along these lines. For example, the arterial flow may be diminished by section of the vasodilator nerves or permanent excitation of the vaso constrictors. If this operation were possible it would enable us to render less active the metabolism of a gland. On the other hand, it is easy to produce a venous hyperæmia by reducing the caliber of the veins. The experiments of Bier showed that venous hyperæmia gives excellent results in the treatment of diseases of the limbs. It would perhaps be true also for diseases of organs, and we intend to experiment along this line. These considerations show that the field of artificial modifications of the circulation is a large one and that a great many experiments must be made in order to determine if such operations may be of practical value.

II. Replantation and Transplantation of Organs and Limbs.

The *replantation* consists of extirpating an organ or a limb with its vessels, of putting it back into place and of re-establishing the circulation by anastomoses of its vessels. Hoepfner experimented with the replantation of limbs (16). We have replanted the thyroid gland (17), the kidney, the leg and the thigh (18) (19).

The extirpation and replantation of the thyroid gland with reversal of the circulation was successfully performed. The right thyroid gland having been dissected, all its vessels were ligated, except the superior thyroid artery and vein, which were cut near the carotid artery and the internal jugular vein. The gland was then extirpated and put in a glass of isotonic sodium chloride solution. After a few minutes, the thyroid gland was placed in the wound in the neck, and the peripheral end of the thyroid artery was united to the central end of the thyroid vein, and the peripheral end of the thyroid vein to the central end of the thyroid artery. The circulation was re-established about half an hour after the extirpation. The circulation through the gland was in a direction reverse to the normal. The red blood entered through the thyroid vein, and the dark blood flowed from the gland to the jugular vein through the thyroid artery. The hue of the gland was normal, and the circulation very active. Eleven days after the operation the wound was opened and the anterior portion of the gland directly observed. The gland was somewhat enlarged, but its hue and consistency were normal. Forty-seven days after the operation, the replanted gland appeared to be practically normal, being only slightly enlarged. Its systolic expansion was easily detected. Eight months after the operation the gland appears to be normal in size and consistency. It was at first superficially located, but it is now much deeper, being about in its normal situation.

The replantation of the kidney was also performed. The right kidney was extirpated, and carefully washed in salt solution. Then it was replaced in the abdominal cavity and the vessels anastomosed. Immediately after re-establishment of the circulation the kidney became uniformly red and clear urine began to flow from the ureter. The ureter was then anastomosed, and the kidney fixed in its normal place. Unfortunately an infection occurred, which resulted in obliteration of the anastomoses and the complete absorption of the organ.

The replantation of the leg was performed on a medium-sized dog. As the vessels were very small the anastomoses produced a stenosis and the circulation was not satisfactory.

On the contrary, the replantation of the thigh always gave an excellent re-estalishment of the circulation. This is an example of this replantation. Through a longitudinal incision the vessels of the thigh were exposed and cut above the point of Scarpa's triangle. The skin was circularly severed and the thigh completely amputated above the junction of its lower and middle third. After a few minutes the limb was replanted. The ends of the bone, the muscles, the vessels and the sciatic nerve were united. The circulation was re-established after having been interrupted for one and one quarter hours. The pulsations of the popliteal and "saphenous" arteries were normal. The dark blood circulated very actively through the femoral and saphenous veins. Red blood flowed from the small arteries of the peripheral part of the cut limb. The skin was sutured and a plaster dressing applied to the limb and trunk. After the operation the general and local conditions of the animal remained very satisfactory. It drank and ate normally and walked on its three sound limbs. The skin of the replanted foot remained normal, but its hue was redder and its temperature higher than that of the normal foot. The anterior part of the foot soon became moderately swollen. Seven days after the operation the dressing was partially removed. The limb presented neither œdema nor trophic troubles. The œdema of the anterior part of the foot was doubtless due to pressure by the lower edge of the bandage, as the swelling completely disappeared within a few hours after correcting the fault of the dressing. The skin was normal and the wound had united "per primam intentionem" without evidence of inflammation. The temperature of the skin was

higher below than above the line of suturing. Eight days after the operation the foot appeared normal in size, all œdema having disappeared. On the tenth day, during the afternoon the temperature of the replanted foot became lower, *i. e.*, similar to that of the normal foot. The dressing was then removed. It was found that, owing to a slipping of the plaster bandage, some urine had got into the cotton dressing and caused infection of the upper part of the longitudinal incision. A small subcutaneous abscess had developed along the vessels. The general conditions of the animal were excellent, and the nutrition of the limb satisfactory. As the arterial pulsations were much weakened and as it was considered important to accurately determine the cause of this change, the animal was etherized and the vessels examined through cutaneous incisions, after which the animal was killed.

This dissection "in vivo" gave the following results: The point of the vascular anastomoses was surrounded by the small subcutaneous abscess. The venous anastomosis was good. The arterial anastomosis was partially occluded by a small clot. All the other portions of the vessels appeared perfectly normal. The circulation through the limb was yet satisfactory, as the obliteration of the anastomosis was not complete. The union of the skin, the muscles and the sciatic nerve was normal. The process of consolidation of the bone was beginning. It is probable, but not certain, that if the animal had been allowed to live, the arterial stenosis would have gradually increased and that in the end the circulation would have been interrupted. Then, no doubt, gangrene of the limb would have occurred, which result would have been due primarily to the secondary infection of the skin. This shows that in such experiments asepsis must be rigidly observed, not only during the operation but during all the postoperative period.

It is permitted to conclude that: (1) The circulation of a replanted limb, re-established an hour and a quarter after interruption, by end-to-end anastomosis of the femoral artery and vein, is normal, as judged by the metabolism of the limb. (2) No trophic trouble occurs (at least during ten days). (3) Healing of the severed tissues appears to be as rapid and complete as after an ordinary surgical wound.

The *transplantation of organs* consists of extirpating an organ with its vessels and grafting the latter onto the circulatory apparatus of the same animal or another animal. This operation may of course be autoplastic, homoplastic, or heteroplastic.

In 1902 I made the transplantation of the thyroid gland with its vessels (20), but it was not possible to observe physiological results, owing to the bad aseptic and technical conditions of the operation. Ullmann (21) made the first transplantation of the kidney by using the method of Payr (22). I was then ignorant of his experiments, and at about the same time (1901-1902) my investigations led me to the same experiments. In 1903 and 1904 similar experiments were made by Carl Beck of Chicago, Höpfner (23), Exner and Costello. In 1905 Floresco (24) continued these experiments and succeeded in transplanting the kidney into the lumbar region. In 1905 Guthrie and I performed the auto and homoplastic transplantations of the kidneys, the supra renal glands, the intestine, the heart, the lungs, the thigh, the ovary, and the heteroplastic transplantation of all the subdiaphragmatic portion of the body.

We use two methods of transplanting organs, *transplantation simple* and *transplantation en masse*.

The *transplantation simple* is the method mainly used. It consists of dissecting out the organ and its vessels and of anastomosing the latter to suitable vessels of the same or another animal. This technique has several drawbacks for the nerves and their sympathetic ganglia are cut off and the veins are unduly exposed to injury. The slightest fault of technique decreasing the caliber of the vessels may dangerously interfere with the circulation to the organ. Besides, it is absolutely impossible to perform the transplantation of organs like the testicle or the ovary on ordinary laboratory animals. For these and other reasons, we looked for a better method. This led to the development of the technique of *transplantation en masse* which consists of extirpating the organs together with its surrounding connective tissues, its nerves and ganglia, and its vessels with the corresponding segments of the large vessels from which they originate. This technique does not preclude injury of the nerves or their ganglia. Also a slight fault of technique in anastomosing large vessels is relatively of little importance. By this method transplantation of the testicle, ovary, suprarenal glands, et cetera, is rendered possible. We employed both methods according to the requirements, in the study of transplantation of organs.

Transplantation of the ovary (25) was performed as follows: The abdomen of a cat A being open, a large peritoneal flap, extending from the right ovary to the portion of the aorta corresponding to the mouth of the ovarian artery, is cut. The Fallopian tube is severed near its fimbriated extremity. The posterior surface of the peritoneal flap is carefully separated from all the posterior tissues excepting the ovarian vessels, which are permitted to retain their connection with it. Then the segments of the aorta and vena cava, from which the ovarian vessels originate, are extirpated. The specimen consisting of the ovary and a part of the Fallopian tube united to the segments of the aorta and vena cava by a peritoneal band and the ovarian vessels, is then placed in a glass of isotonic sodium chloride solution.

The abdomen of another cat (cat B) is then opened by performing a right, half-circular, transversal laparotomy. The right ovary and the external part of the Fallopian tube are resected. The aorta and vena cava are cut at the point of the mouth of the ovarian vessels. The anatomical specimen taken from cat A is removed from the salt solution and put into the abdominal cavity of cat B. The segments of the aorta and vena cava of cat A are interposed between the cut ends of the aorta and vena cava of the cat B. The peritoneal flap is attached to the posterior abdominal wall in such a manner that the transplanted ovary takes the place

of the normal ovary. The circulation through the aorta and vena cava is re-established. The red blood traverses the ovarian artery, the ovary becomes red, and the dark circulation is slowly established through the venous plexus and the ovarian vein. After a few minutes the circulation appears similar to that of the normal ovary. The end of the transplanted Fallopian tube is united to the end of the normal one. At last the suture of the abdominal wall is performed.

This operation is not very dangerous, for the animals a few hours after recovering from their anæsthesia appear to be in normal condition. Our experiments were performed on ordinary vagrant animals of uncertain breeds. They are only instructive, therefore, from a technical point of view. We intend to very soon perform a series of similar operations on pure breed animals, preferably dogs or pigs, with a view of studying the problem of transmission of characters and related problems.

The same procedure may be used for the transplantation of the testicle, and it would be better to use the method of patching instead of the biterminal transplantation. This transplantation of the ovary or testicle may be used for the study of the internal secretions by the multiplication of organs, for instance putting several testicles on the same animal or a large testicle on a small dog.

In the transplantation of the thyroid gland we used the simple method of transplantation. It might be useful to employ the method of transplantation *en masse* or by patching.

The *transplantation of a loop of intestine* into the neck was made as a preliminary study of the substitution of such a tube for the œsophagus. A segment of intestine was resected with its mesentery and vessels. The loop of intestine was put into the neck and its vessels implanted on the wall of the jugular vein and of the carotid artery. Soon after, the circulation was re-established the intestine assumed its normal hue. There appeared to be no vaso-dilatation, and twenty minutes later peristaltic movements were observed. They were spontaneous and easily exaggerated by mechanical excitation. The appearance of the bowel was entirely normal. Then its ends were sutured to the skin, and the wound closed. Unfortunately a phlegmon of the neck developed the following day, and it was necessary to extirpate the loop of intestine.

The *heart was* transplanted in several different ways. This is an example (26): The heart of a small dog was extirpated and transplanted into the neck of a larger one by anastomosing the cut ends of the jugular vein and the carotid artery to the aorta, the pulmonary artery, one of the venæ cavæ and a pulmonary vein. The circulation was re-established through the heart, about an hour and 15 minutes after the cessation of the beat; 20 minutes after the re-establishment of the circulation, the blood was actively circulating through the coronary system. An opening made through the wall of a small branch of the coronary vein led to an abundant hemorrhage of dark blood. Strong fibrillar contraction soon occurred. Afterward contractions of the auricles appeared, and, about an hour after the operation, effective contractions of the ventricles began. The transplanted heart beat at the rate of 88 per minute, while the rate of the normal heart was 100 per minute. A little later, tracings were taken. Owing to the fact that the operation was made without aseptic technic, coagulation occurred in the cavities of the heart after about two hours, and the experiment was interrupted.

We attempted also to make the *transplantation of the lungs together with the heart.* Both lungs, the heart, the aorta, and vena cava of a cat one week old were extirpated and put into the neck of a large adult cat. The aorta was anastomosed to the peripheral end of the carotid, and the vena cava to the peripheral end of the jugular vein. The coronary circulation was immediately re-established and the auricles began to beat. The lungs became red and after a few minutes effective pulsations of the ventricles appeared. But the lungs soon became œdematous, and distention of the right part of the heart occurred. This accident seems difficult of prevention. A phlegmon of the neck terminated this observation two days later.

The transplantation of the *suprarenal glands* was performed at the same time as the transplantation of the kidneys. From a macroscopical standpoint, it seems to be successful, but histological examination has not yet been made.

We performed the *autoplastic and homoplastic transplantation of one or both kidneys.* The kidney of a small-sized dog was extirpated and transplanted into the neck (27). The renal artery was united to the carotid artery, the renal vein to the external jugular vein and the ureter to the œsophagus. Three days after the operation the neck and the abdomen were opened, in order to study the functions of the transplanted kidney and to compare them with the functions of the normal kidney. The transplanted kidney was found adherent to the muscles, and dissection was necessary to free it. In size it was larger than the normal kidney. Its hue was darker. To the touch the consistency of its tissue was normal, and the pulsations of its artery were as strong as the pulsations of the artery of the normal kidney. The circulation in the transplanted kidney was slightly greater than in the normal kidney, as detected by the touch, copiousness of hemorrhage from incision in cortex, and pulse-tracings. The secretion of urine by the transplanted kidney was about five times more rapid than by the normal one. The intravenous injection of sodium chloride solution caused no change in the rate of secretion in the normal, but markedly increased the rate of the secretion in the transplanted organ. The composition of urine secreted by the transplanted kidney differed somewhat from that secreted by the normal one. The constituents were similar, but the chlorides appeared to be more abundant in the urine from the transplanted kidney, while the organic sulphates, pigments and urea were more abundant in the urine from the normal organ.

The autoplastic transplantation of the left kidney on the right side, after extirpation of the right kidney has been performed once. But infection immediately occurred producing

peritonitis, obliteration of the vessels, uremia, and death forty hours after the operation.

The homoplastic transplantation *en masse* was performed as follows (28): Both kidneys and the upper part of the ureters, together with their vessels, nerves, nervous ganglia, the surrounding connective tissue, the suprarenal glands, the peritoneum and the corresponding segments of the aorta and vena cava were removed. The mass was then placed in a vessel of isotonic sodium chloride solution. The aorta and vena cava of another animal were cut a little above the mouth of the ovarian vessels. The kidneys of the first animal were then removed from the salt solution and put into the abdominal cavity of the second, and the segments of the aorta and vena cava were interposed, by biterminal transplantation, between the cut ends of the aorta and vena cava. The circulation was re-established, after having been interrupted for one hour and a half. The kidneys immediately became red and turgid, as after a simple transplantation, but about half an hour later the state of the circulation became normal, so that no difference could be detected between the transplanted and the normal kidneys. Clear urine flowed abundantly from the transplanted ureters, which were united to the normal ones.

Both normal kidneys were dissected free and extirpated. The operation was completed by suturing the abdominal wall and applying the dressing. Two hours after the operation the animal walked about her cage. In the afternoon she drank and urinated copiously. The following day and subsequently, up to the eighth day, her diet consisted largely of meat, which she took hungrily. In general her condition was normal. During this period the urine remained clear, showing no evidence of containing blood. The total amount appeared to be somewhat increased. On the seventh and eighth days several samples were collected and analyzed, the results of which showed a slight variation in composition, but entirely within normal limits. The only abnormal constituent detected was coagulable proteid, the largest amount present in any of the samples being less than 0.25 per cent.

On the ninth day she began vomiting. A diagnosis of stenosis of the bowels by adhesions was made. On the tenth day the urine was analyzed and its composition was practically the same as before. As the animal was almost continuously vomiting, she was etherized and a laparotomy performed. We found localized peritonitis on the right side of the abdomen, with kinking of several loops of intestines, the mass being very strongly bound down by adhesions. The circulation of both kidneys was found to be perfect. There was an enormous hydronephrosis on one side.

We attempted to study the results of *heteroplastic transplantations of organs* from one species to another, but the experiments were unsuccessful and before making other attempts we intend to try to immunize the organs of an animal against the serum and organ extracts of another animal. On account of cytolysins it seems improbable that indiscriminate heteroplastic transplantation can be successfully performed. The transplanted organ must be prepared to support the serum of the animal on which it is to be grafted. We do not yet know if such immunization is possible.

C. Clinical Applications.

As yet it would be improper to draw definite conclusions from these experiments, for they are too incomplete. Therefore I would like to omit this part of the subject. But as immediate continuation of this work is doubtful, I shall briefly speak of its possible relations, first to the actual surgery of blood-vessels (26), and secondly to the surgery of organs and limbs.

I am very far from affirming that our plastic operations on blood vessels will on man give as good results as we have obtained on cats and dogs. Successful experiments on such animals do not warrant the drawing of definite conclusions as to their adaptability to man. The conditions as regards the vessels and the blood are different. The results would be doubtful if the operations were made on atheromatous arteries, sclerotic veins, or tissues of diathesic patients.

Nevertheless the use of our improved technic may be of value in all the actual operations on blood vessels (29). Thrombosis following the operations on blood vessels are due often to methods which do not properly meet the conditions for the continuation of the physiological processes. Therefore the results of the present blood-vessel surgery will be enhanced by the use of our methods of temporary hemostasis, of handling the vessels, of washing them with isotonic sodium chloride solution, of impregnating the threads and coating the vascular wall with vaseline, of exactly approximately the internal layers without invagination, and of suturing with very fine needles while the wall is somewhat stretched.

Some of the plastic operations may lead to the establishing of new therapeutic methods. For instance, the ideal treatment of large wounds of arteries and of aneurisms would be the extirpation of the diseased portion and the immediate re-establishment of the circulation (30). Hitherto, in exceptional cases the continuity of the artery has been re-established by end to end suturing. This is generally impossible on account of the gap between the cut ends of the vessel. But the continuity of the vessel would very easily be re-established by the biterminal transplantations of a vein or of an artery. After having extirpated an aneurism, it is possible to interpose between the cut ends of the artery a segment of the neighboring vein, or of some other vein, the saphenous or the external jugular for instance. If heterotransplantation prove successful, it may be possible to interpose between the cut ends of the vessel a segment of a vessel of a lower animal, *e. g.*, hog. This would annul the risk of gangrene following the extirpation of aneurisms. The other applications of these methods to the vascular surgery are so simple that they do not need description.

I shall briefly sketch their hypothetical applications to general therapeutics.

It is probable that the present surgery of organs is yet in its infancy. It consists mainly of section or of extirpation.

For example, when a kidney is inflamed a nephrotomy is performed. If the lesions are more serious, it is resected. When other organs less essential to life are diseased often they are extirpated without thought as to their physiological functions. It is not unreasonable to believe that, instead of cutting and extirpating a diseased organ, it may be possible to influence favorably its nutrition by operating on its vessels or nerves. On the other hand, when the extirpation of an organ is necessary the ideal treatment would be the immediate transplantation of a sound organ to take its place. Let us examine briefly these two hypotheses.

I. The nutrition and the functions of organs and tissues depend on their circulation and their excitator nerves. An increase of the circulation modifies probably the formative and productive power of tissues. It is reasonable to suppose that by increasing the metabolism activity of a diseased organ, it may be strengthened and enabled to overcome or to limit the morbid processes. We obtained an increase of the red circulation of the skin or of organs by acting on the blood vessels directly or through their vaso-motor nerves. The transplantation of a large vein into an artery produces a strong arterial hyperemia which seems entirely without harmful influence. Unfortunately we had no opportunity to use this method on organs presenting chronic or acute inflammation. It was applied only to benign growths of the thyroid gland, in which case it rapidly alters the anatomical structure, and appears to increase the glandular activity. If subsequent experiments demonstrate the constancy of these results, it should be possible with slight technical modification to use this method on man. Operations acting on the vaso-motor nerves alone are also able to cause an increase of the red circulation. Temporary denervation of organs, or stretching or crushing of their nerves is easier to perform than the operations on blood vessels, but may be more dangerous, at least for certain organs. These operations which consist in the simultaneous cutting of the vaso-motor and excitator nerves are of course very imperfect. Nevertheless they produce strong arterial hyperemia, and, on some organs, like the thyroid gland and the ovary, are probably harmless. It is known that section of all the nerves of the thyroid gland is followed by a temporary vaso-dilatation and that it does not produce any histological modifications of the cells. Our own experiments demonstrate that eight months after the extirpation and replantation, the thyroid gland is apparently normal in size, consistency and circulation. I have examined microscopically the section of an ovary of a chicken about fourteen months after it was transplanted by Guthrie. Its histological appearance was absolutely normal. Also it is known that the functions of a transplanted ovary may be completely re-established. For these many reasons we consider the denervation of the thyroid gland and the ovary as not dangerous. As regards the ovary, it would probably be better, from a physiological standpoint, to make the denervation rather than the resection of the organ, in a case of chronic inflammation.

In case of disease of the kidney, Bright's disease, for instance, the question is more complicated and cannot be settled at the present time. It is certain that complete denervation is harmful. However, the physiological experiments of De Vecchi showed that rabbits will survive after cutting all the nerves of both kidneys, though degenerative changes of the cells of the tubules were observed by him a few days after the operation. On the other hand, the urine of a transplanted kidney was almost normal ten days after the operation, and the animal did not present symptoms of uremia. For these reasons, I believe that the temporary denervation of the kidney is not very dangerous, but that it should not be used on man, at the present time. Partial denervation would be less dangerous. In a case of Bright's disease, in which medical treatment had failed, my friend Dr. Carl Beck, of Chicago, partially denervated one of the kidneys. Before the operation the amount of urine for 24 hours was 180 cc., and the urea less than 1 gm. for 100 cc. After the operation the amount of urine and urea became about 550 cc. and 15 g. respectively. Fifteen days after the operation the amount of urine was above 1000 cc. and the urea normal.

No conclusions, of course, must be drawn from this single observation, and, even if temporary denervation may yield successful results, we shall attempt to find some other operations producing vaso-dilatation of the organ without cutting of the nerves.

II. Clinical applications of the transplantations of organs are so obvious that they do not need to be described. If I were a veterinary surgeon and had to treat a myxœdematous dog, I would not hesitate to transplant into its neck a thyroid gland from another dog. In a case of a dog presenting Bright's disease, it would be a rational procedure to substitute for one of his kidneys a sound kidney extirpated from some normal dog. This operation would probably give good results, if performed on large-sized dogs and in a proper operating room. But the question of the transplantation of organs on man is difficult and very far from settled. In the first place, it is necessary to be sure that a transplanted organ may live in good condition after a very long time. This will be established only when a dog bearing the thigh or kidneys of another dog will have been kept in perfect health for years. Secondly, the difficulty of finding organs suitable for transplantation on man must be met. As regards the limbs, in which the tissues remain viable for a long time after interruption of the circulation it would be possible to use, immediately after death, the cadaver of an executed criminal or of a man killed by accident. It is not unreasonable to believe that some transplantations, as, for instance, the transplantation of the arm a little above the elbow, may be successfully performed if an adequate technique is used. As regards the kidneys, the thyroid and the glands in which the endothelium is easily injured by a short interruption of the circulation, the problem is more complex. For, if a limb can be separated from the body for several hours without great damage to its tissues, the same is not the case with a kidney. Then it would be extremely difficult to have an organ to transplant in good condition. In some exceptional cases it

would be possible perhaps to use the kidneys of a man killed by accident. Also the organs of the anthropoid apes are perhaps able to tolerate human plasma. But nothing precise is known in that respect. Besides, anthropoid apes are very expensive, and difficult to handle. Their use would probably be impracticable. The ideal method would be to transplant on man organs of animals easy to secure and to operate on, such as hogs, for instance. But it would in all probability be necessary to immunize organs of the hog against the human serum. The future of transplantation of organs for therapeutic purposes depends on the feasibility of heterotransplantation. Researches must be directed along this line, but as yet we have not been able to do more than perform a few preliminary experiments.

I must apologize for presenting such an important subject as this portion of the surgery of the blood vessels is, in a so superficial manner. The incompleteness of the experimental work is due, not so much to the difficulty of the experiments themselves as to the unsuitable surroundings in which they have been made. A great many other operations must be performed. Their results will indicate whether or not these researches may, in their limited field, contribute to the progress of the medical sciences.

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THE BLOOD OF NORMAL YOUNG ADULTS.

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During the past few years we have collected a series of records of blood examinations which are, we believe, the equal in accuracy of any yet published, and therefore of interest to report. We refer to the blood examinations made by our students of their own or of their classmates' blood during the course in clinical microscopy and clinical chemistry. This course is a part of the third year curriculum. Considerable work is done outside of class hours, and this includes practice with various blood instruments until they have become familiar and have attained a high degree of accuracy with their use.

It may seem, after reading this article, as if we allowed this practice with blood instruments to take too much time, and demanded an accuracy which was unnecessarily exact for clinical use. We know that during their fourth year as clinical clerks our students will not take half the time for a blood examination that they do during their third year, and that any method to be of clinical value must be brief. But only he can do quick work of even approximate accuracy who has previously done slow accurate work with this or a similar method. Hence, during their third year our students practice on themselves and on each other, handing in reports of the work done. Many students of the past five years attained a high degree of accuracy and experimented further, making many observations of considerable value. It is on these studies that this paper is based.

RED BLOOD CELLS.—The statement is commonly made that the red-blood-cell count of a normal man is 5,000,000, and of a normal woman, 4,500,000 cells per cubic millimeter. One gets the idea that these are fairly fixed values with normally rather narrow limits of variations, much as is true of the temperature, and, hence, one is often surprised at the variations in blood counts.

Our students practice counting as follows: The blood is taken from the ear, the finger or the forearm, in the latter case an area without pain-point over a vein being selected. Great care is taken that the part chosen is not cyanotic from position or pressure. The Thoma-Zeiss apparatus is used, with Toisson's fluid as diluent, and in a dilution of 1 to 200. The students make with each mixture two counting chamber preparations and count on each four, usually the corner, units. A unit consists of twenty-five small squares, or one-sixteenth of a square millimeter. Hence, eight units or one-half a square millimeter are counted from two drops of the mixture. Twenty-five cells is the greatest difference allowed between any two of these eight units. Good mixing in the pipette insures that the two drops should agree closely, and careful spreading on the slide that the four corners of each should be nearly uniform. The student makes a preliminary series of counts to familiarize himself with the method, and then starts a series, counting on successive days at the same hour each day, until the difference between two successive days is not over 200,000 cells. At the same time the above mentioned agreement of units must be obtained. This latter requirement of units is the more exacting of the two, for if that is fulfilled on two successive days the two total counts will usually fall well within the 200,000 cell unit, and to require 100,000 cells as the maximum difference would not be a much more difficult task for the student, as a glance at the following table will show. In the records of the blood examinations of 172 students, men and women, there was stated just what the difference between the counts of the two successive days was.

TABLE I.

Difference between counts of two successive days.	Number of cases.
0 to 20,000 red cells	25
20,001 to 40,000 " "	26
40,001 to 60,000 " "	28
60,001 to 80,000 " "	33
80.001 to 100,000 " "	23
100,001 to 120,000 " "	12
120,001 to 140,000 " "	10
140,001 to 160,000 " "	5
160,001 to 180,000 " "	6
180,001 to 200,000 " "	4

Thus the differences in 135 or nearly 80 per cent of the cases were 100,000 or below, and the mean of all was 64,200 cells.

We wish to report the red cell counts made on 171 students, all young men, and all in good health. Their ages were as follows:

TABLE II.

20 and 22 years	2
23 and 24 "	50
25 and 26 "	62
27 and 28 "	37
29 and 30 "	8
31 and 32 "	3
33 and 35 "	2
Doubtful	7

In the case of 150 students the records are perfectly complete and hence there is no doubt but that the counts answered the specifications required above. These 150 constitute Group A, Table III. We have little doubt but that the records of the other 21 are as accurate as these, and report the whole 171 as Group B. To show how little influence age between the years 20 and 35 has over the count, we have grouped the

149 students between 23 and 28 years of age as Group C. The averages of the two counts on the successive days are here reported.

TABLE III.

Red cells per cubic millimeter.	Groups A		Groups B		Groups C	
4,500,000 to 4,700,000	1		1		1	
4,700,001 to 5,000,000	6		8		8	
5,000,001 to 5,200,000	22		22		18	
5,200,001 to 5,400,000	22		25		25	
5,400,001 to 5,600,000	31		35		30	
5,600,001 to 5,800,000	32	84%	38	83.5%	31	82.5%
5,800,001 to 6,000,000	19		22		19	
6,000,001 to 6,200,000	9		10		8	
6,200,001 to 6,400,000	3		4		4	
6,400,001 to 6,600,000	2		2		2	
6,600,001 to 6,800,000	3		3		3	

The physiological limits for the counts for normal young men, as judged by our students in this climate, and during the months of October to February, are 4,500,000 and 6,800,000. In the case of over 82 per cent of the cases examined the limits were 5,000,000 and 6,000,000, while for 45 per cent, or nearly one-half, the counts lay between 5,400,000 and 5,800,000. The mean count, that is, that figure around which most counts lie, and which is not influenced by the extremes, as is the average, was, for Group A, 5,440,000; Group B, 5,430,000, and Group C, 5,454,000. Our "average" student, therefore, has a count of about 5,440,000; yet it does not mean that the student with 4,500,000 red cells was necessarily anæmic, nor that he with 6,800,000 was necessarily polycythæmic. These counts were apparently normal for those men at that time.

The count if taken at the same hour each day over short periods of time is remarkably constant. The following are the counts of one student on eight consecutive days:

5,180,000	5,136,000
5,104,000	5,060,000
5,000,000	5,140,000
5,184,000	5,000,000

Over longer periods of time, however, the count may vary much. The statement is made that the variations between summer and winter are considerable. We have no counts to test this, since our work is all in the fall and winter, yet the following cases would indicate such variations.

L.	Oct. 26	5,212,000
	27	5,296,000
	28	5,160,000
	Dec. 8	5,524,000
	9	5,532,000
H.	Nov. 27	4,656,000
	28	4,556,000
	Dec. 20	4,812,000
	21	4,784,000
	22	4,832,000
P.	Dec. 3	5,764,000
	4	5,728,000
	Jan. 15	5,932,000
	16	5,928,000

And others show no such changes.

S.	Nov. 18	5,816,000
	19	5,772,000
	21	5,856,000
	22	5,824,000
	Jan. 10	5,620,000
	11	5,688,000
V. d. H.	Nov. 7	5,532,000
	Dec. 10	5,424,000
	11	5,485,000

HÆMOGLOBIN.—The estimation of hæmoglobin is theoretically more valuable than the red count, since it is much more quickly and easily done. Theoretically, also, it should be more accurate, but as a matter of fact it is the most inaccurate part of our blood examination, and it is the instruments which are to blame for this.

The experience of this clinic is as follows: Formerly one make of instrument (v. Fleishl) was used on all the wards. Every one was satisfied for the results were comparable, but they were not correct. Then four different kinds of instruments (Fleishl, Miescher, Gowers, Dare) were put in use, and the ward workers trained to be skilled in the use of all. The readings were often ridiculously different, evidence of the inaccuracy of the several instruments, and yet the results were salutary. The men learned the weak points in each instrument. Then the same makes were kept in use, but all standardized to one particular instrument, a Miescher. The results were at once better. Our tendency now is to return to one form of hæmoglobinometer. All the several instruments will be regulated with one accepted as the standard. We are now experimenting with the new Sahli hæmometer in hopes this will prove satisfactory. At present it is not, since the instruments read even 30 per cent too high, but that is a simple matter of restandardization.

The essential points in a satisfactory hæmoglobinometer are: simplicity, a one-color standard, convenience and speed in use, and a reduction in value of the personal equation. The maker may mark it as he will, (and he does it poorly), but it should not be difficult to restandardize it to a fresh solution of hæmoglobin. Instruments requiring fifteen to thirty minutes for a determination, or a dark room are almost prohibited; those with color prisms are too hard to standardize and hence to restandardize. The Tallqirst allows too much of the personal element to enter, and we look forward to an instrument taking only a little longer and allowing readings correct to within 2 to 5 per cent.

Whatever instrument is chosen it should be one reading "grams" and not "per cent." Weight is something which we can understand and verify; per cent means relation to normal, the latter expressed as 100. But how does this work out? In the first place, there is no hæmoglobin content which is normal for all ages. Normal for a child would be too low for an adult. To say that a child, using an instrument reading 100 for adults, has 80 per cent hæmoglobin suggests that the child is anæmic, whereas that figure expresses an amount which is normal (that is, 100 per cent) for the child. Again,

who is to say what is normal? It must be a certain weight of hæmoglobin per 100 ccs. of blood. But one instrument is standardized using the color of a 13.7 gms. per 100 ccm., another a 14 gms., and still another a 14.5 gms. solution, and one confessed to having used a 17 gms. solution to determine the 100 point. Evidently 100 per cent is a pretty variable point and we do not wonder that the same blood at the same time can on different instruments read both 90 and 120. Since the makers must (or claim to, although we often doubt they take the trouble) make up a hæmoglobin solution of known weight per cent, why can they not state this weight on their instruments? Why not mark the scales off in grams, leaving us to decide whether the reading of a given blood is normal, *i. e.*, 100 per cent, or not? Examination of our figures might lead one to question whether or not our instruments really varied so much. The reason ours agree as well as they do is that of the eight or more instruments of various makes bought each year, we have to send back sometimes one-half to be replaced by others better standardized. This a practitioner buying but one would hardly do.

And, lastly, we want an instrument in the use of which the personal equation is not the important factor. We can all guess percentages. We know men whose guesses from a drop of blood on a rag, and the Tallquist scale is only a refinement of this method, are fairly accurate. But an error of 10 to 15 per cent is too great to be satisfactory to most careful workers. No one would now allow a real cell count to be stated as "75 per cent of normal." We demand the count itself. So we should demand the actual amount of hæmoglobin, and the latter should be as accurate or more so than the former.

A study of our students' reports of their bloods, using these various instruments, is of interest.

	Dare	Fleishl	Gowers	Tallqirst
65 to 70	1	3	3	
70 to 75	1		2	
75 to 80	8	9	5	1
80 to 85	10	20	13	9
85 to 90	23	25	14	14
90 to 95	50	52	46	33
95 to 100	51	32	36	34
100 to 105	3	11	16	
105 to 110	4	5	7	
110 to 115		3	2	
115 to 120	1		2	

With the Dare instrument 152 bloods were examined. Of these 101 lay between 90 and 100 per cent, and the mean figure was 93 per cent.

With the Fleishl instrument 158 bloods were examined. These varied somewhat more than those with the Dare, 129 lying between 80 and 100 per cent, and the mean of all was 92 per cent.

With the Gowers instrument 146 bloods were studied. Of these 82 lay between 90 and 100 per cent, and the mean of all was 94 per cent.

With the Tallqirst scale 91 determinations were made, with a mean of 93 per cent. It might seem at first sight as if the narrow limits of these last figures indicated the accuracy of this method. We consider it quite the reverse, that subjectively the observers have raised the values to nearly 100 per cent the "normal value."

The Miescher modification of the Fleishl instrument is, we are sure, the most accurate of the instruments mentioned. This is not an instrument for ordinary clinical use since it takes too much time, a dark room, and too much practice. This is the best instrument by far to train the accuracy of the students in color work, since the results are so well controlled. Our students examine the same blood by this method on two successive days at the same hour each day. A difference of 0.2 gms. was allowed. We have 121 such records and use here the average of the two determinations.

11 to 11.9 gms	2 students.
12 to 12.9 gms	7 "
13 to 13.9 gms	16 "
14 to 14.9 gms	35 "
15 to 15.9 gms	30 "
16 to 16.9 gms	25 "
17 to 17.9 gms	6 "

The majority, 106 bloods, read between 13 and 17 gms. The mean was 15.13 gms. It will be noticed that by this method the variations are the greatest. One would expect this since the variations in the count are great, hence those in hæmoglobin are probably as great.

Color Index.—This most valuable figure is the quotient of the hæmoglobin per cent, the numerator, and the red-cell per cent (5,000,000 as 100 per cent) denominator. For a normal person this should be 1. But using the figures of our "average" student, it is with the Fleishl instrument 0.86, with the Dare, 0.88, and with the Gowers, 0.87, all of them being values which are usually considered distinctly "chlorotic." We believe the color index could be more correctly expressed in terms of the amount of hæmoglobin per one million cells. We asked some of our students to so arrange their work that a count and hæmoglobin estimation with the Miescher instrument could be made on the same blood at the same time. We have records of but 21 different bloods examined in this way with several determinations on each blood, but they are quite enough. We give here the average for each student.

Grams of Hb. per 1,000,000 cells.	Number of cases.
2.20 to 2.39 gms	4
2.40 to 2.59 gms	5
2.60 to 2.79 gms	8
2.80 to 2.99 gms	3
3.43 gms	1

The mean of these is 2.68 gms., and the average is 2.63 gms. It is interesting that while the weight per corpuscle in different persons varies somewhat, the values found in the same person at different times vary but little, even though the absolute values of cells and hæmoglobin vary considerably.

The following figures are the values in students found at fairly long intervals.

Sl.	3.43	3.45	3.41
H.	2.80	2.83	
P.	2.72	2.71	2.77
Wi.	2.66	2.69	
We.	2.39	2.38	
Ki.	2.90	2.96	

These are few of many illustrations. Accepting the figure 2.65 as the average weight per 1,000,000 cells we propose to use this as the denominator of a fraction, the numerator of which is the corresponding value for the case in question. For a practical illustration of this the reader is referred to the report by Mr. Wroth, who very kindly followed a few cases in this clinic. This paper will appear in a forthcoming number of the Bulletin.

Leucocytes.—The question of the leucocyte count of the normal person is a more difficult one to handle, since this varies within such wide limits. We required each student to make three counts: one with Toisson fluid, dilution 1:200; one with acetic acid (1 per cent), dilution 1:100; one with this same acetic acid, dilution 1:20. Counts on one blood at the same time by these three methods vary but little. We give the highest and the lowest counts in the case of 167 students.

Lowest counts:

2,000 to 4,000	2	students.
4,000 to 5,000	12	"
5,000 to 6,000	25	"
6,000 to 7,000	48	"
7,000 to 8,000	45	"
8,000 to 9,000	26	"
9,000 to 10,000	4	"
10,000 to 13,000	5	"

The mean count of this group is 7000.

Highest counts:

4,000 to 5,000	1	student.
5,000 to 6,000	9	students.
6,000 to 7,000	17	"
7,000 to 8,000	42	"
8,000 to 9,000	34	"
9,000 to 10,000	35	"
10,000 to 11,000	12	"
11,000 to 12,000	12	"
12,000 to 13,000	4	"
14,000	1	student.

The mean of these counts is 8400.

We, therefore, conclude that for our students the "average" leucocyte count is between 7000 and 8400.

Counts in Women.—We have records of the blood of but 16 women students examined in just the same manner as in the case of the men. The ages of these women varied from 22 to 32 years.

The red counts were:

4,300,000 to 4,500,000	3	students.
4,500,000 to 4,700,000	5	"
4,700,000 to 4,900,000	2	"
4,900,000 to 5,100,000	5	"
5,300,000 to 5,500,000	1	student.

The hæmoglobin estimations, the mean values given, were: Miescher, 11 gms.; Dare, 87 per cent; Gowers, 82 per cent, and Fleishl, 85 per cent. Their lowest leucocyte counts varied from 5000 to 13,000, the mean being 7100; the highest from 5000 to 16,000, the mean being 9500.

NOTES ON NEW BOOKS.

The Eye and Nervous System. Their Diagnostic Relations by Various Authors. Edited by Wm. Campbell Posey, A. B., M. D., Professor of Ophthalmology in the Philadelphia Polyclinic, Surgeon to the Wills Eye Hospital, etc., and William G. Spiller, M. D., Professor of Neuropathology and Associate Professor of Neurology in the University of Pennsylvania, etc. Illustrated. (*Philadelphia and London: J. B. Lippincott Company, 1906.*)

With the exception of Wilbrand and Sänger (Neurologie des Auges) nothing like the present volume has been presented to the profession within later years. The work of Wilbrand and Sänger is not the only one which has appeared on this subject in Germany, but in this particular field of medical literature it leads all others in completeness, not only in its own country but elsewhere. So far as we know "The Eye and Nervous System," by Posey and Spiller, is the only work of the kind in the English language. That it was needed seems reasonably certain and that it will meet with favor among a limited few is likely. It will be read by ophthalmologists and neurologists, especially by the latter, but it will not find its way certainly to any great extent into the library of the general practitioner. The volume contains not far from a thousand pages and consists of a series of monographs (twenty-four in all) by various authors. A work from the hands of several of the best ophthalmologists and neurologists in this country is apt to be of a high order and we regard it as such. The aim of the editors has been to present ophthalmo-neurology in such a manner that the general practitioner may without difficulty become conversant with its symptomatology; they have been aided in their efforts to do this by men who have distinguished themselves in these two branches of medicine. Although this aim is truly worthy we doubt the expediency of introducing so much material that is purely technical or scientific as opposed to that which is clinical or practical, for while the reader gains a more exhaustive treatise he becomes burdened with much that appeals neither to his understandings nor his sympathies.

We notice here and there careless spelling. Whatever simplification of spelling methods the future may have in store for those who dwell within the boundaries of these United States there is as yet no excuse for blundering over such names as Strümpell (page 649), Hirschberg (page 554), Shumway (page 536), and such a word for example as *sequelæ* (page 737).

These, however, are blemishes which do not materially mar the intrinsic worth of a work which contains a vast amount of valuable information and which testifies to the enterprising char-

acter of the School of Ophthalmology which has flourished so long and so honorably in Philadelphia.

Primer of Psychology and Mental Disease. By C. B. BURR, M. D. Third edition. (*Philadelphia: F. A. Davis Company, 1906.*)

It is always a pleasure to note the success that an author has with his book, and the call for a third edition of this primer is evidence that it has been helpful to those students to whom it is addressed. It is a most difficult task to condense into such small space the two broad subjects of psychology and insanity, but the author has presented them in a clear and succinct form, and one which makes easier for the student who desires to study further along these lines to understand the larger and profounder works which deal with these topics. Not having the first two editions at hand it is impossible for the reviewer to compare this last edition with the earlier ones, but this seems unnecessary in that the primer as it now appears is well adapted to its end. The only criticism to be made is in regard to the author's use of English, and if a fourth edition is called for, as it is to be hoped may be the case, it will be easy for him to make the necessary corrections, which are but few in number; such lapses as the use of "recoverable" for "curable," and "soluble" for "loose," are mere evidences of hasty writing and do not diminish the intrinsic value of the book. R. N.

History of the Boston City Hospital, 1864-1904. Edited by a Committee of the Hospital Staff. (*Boston: Municipal Printing Office, 1906.*)

A city hospital which for forty years has been managed so honestly and capably, with "politics" interfering and hampering its administration but little, deserves to have its history written, and it is a pleasure and interest to read this book. In it is to be found not only a full description of the hospital and its growth in size and production, but reminiscences of trustees, doctors, house officers, and nurses who have worked in the hospital; the most complete history of its sort perhaps on record. So many able and well-known physicians and surgeons have been connected with the City Hospital, and so much excellent work has been done within its walls, that these men deserve to have their work and name commemorated in this pleasant manner. The men and their work are the best proof that a city hospital, free from "politics," can produce as good work as a private hospital, and it is to be hoped that "politics" will never get the upper hand in this hospital. Not alone Boston, but Massachusetts and the other States may be proud of the City Hospital. R. N.

The Harvard Medical School, 1782-1906. (*Privately printed by the Medical Faculty, 1906.*)

As a fitting close to the interesting ceremonies at the dedication of the new buildings for the Harvard Medical School, the faculty of the school has issued this most handsome volume. The history is presented in a brief account of each department, arranged in chronological order, with a protrait of the first occupant of each chair—"provided he be not now alive,"—only one portrait is lacking in this series of noteworthy physicians, that of Dr. Aaron Dexter, the first Professor of Chemistry and Materia Medica. There are also illustrations of the different buildings which have housed the school since its commencement, 124 years ago, which mark, as perhaps nothing else would, the growth of medicine, as a science and profession, since the end of the eighteenth century. Such a history will be valueless a hundred years hence, and the faculty of the Harvard Medical School is to be most warmly congratulated on its publication.

R. N.

A Statement of Facts and Explanations on Leprosy and Fish-Eating. By JONATHAN HUTCHINSON, F. R. S., LL. D., formerly President of the Royal College of Surgeons. (*London: Archibald Constable & Co., Ld.; Chicago: W. T. Keener & Co., 1906.*)

This remarkable book, not only remarkable but extremely interesting, is the elaboration of a theory which the renowned author has upheld for fifty years. As he asserts in the preface it is not only written for medical men but also for the public, especially those who live in countries where leprosy occurs. The purpose of the book is to bring forward a mass of evidence which is both historical in character and also the result of wide and extensive personal observation in Europe, India, and South Africa, the effort being to demonstrate that leprosy is brought about chiefly by the eating of fish in a state of decomposition or badly cured.

The author shows further that leprosy is not contagious by touch, that segregation is and has always been totally insufficient to suppress the disease and has never caused it to decline. He also asserts that whenever there is plenty of salt in the curing of fish there is no leprosy.

As the result of careful investigation the author demonstrates that this disease is most prevalent in islands and along the shores of continents. In Norway where leprosy is and has always been for many generations prevalent the natives prefer to eat fish in a state of partial decomposition.

After the discovery of the bacillus of leprosy by Hansen, Hutchinson hoped this organism would be found in fish, but it has not yet been found in them; evidence however has been collected, according to the author, to prove the fish theory without demonstrating the presence of the bacilli in fish.

The author discusses all the theories about contagion and the occurrence of the disease in persons who have never eaten fish, and finds that most of the statements supporting the latter contention are not to be relied on and that the very large majority of the cases all the world over are most probably to be explained by his fish theory. The author has to explain some undoubted cases of leprosy in which it could not be proven that fish had ever been eaten; in these cases he thinks the disease was due to eating food which had been handled by lepers. He calls this the "indirect" or commensal method, which also explains why the disease is apt to cling to certain families and run in successive generations.

The attempt to isolate lepers always has been, he says, and always will be illusory.

The author practically discusses, in this work, the subject of leprosy in a most entertaining and lucid manner from every standpoint, its origin, its antiquity, its symptoms, its distribution, etc.

He declares leprosy is not necessarily fatal, but that it may be averted at any stage, and if all lepers were liberally fed and properly cared for few would probably die of this disease.

The author makes some rather startling statements, for example (page 31), that leprosy and tuberculosis are allied diseases, as both are well nigh ubiquitous, and are actively propagated by the use of special foods. He also suggests that the bacillus of leprosy and the tubercle bacillus may have a common ancestry. He does not believe in the theory that tuberculosis spreads by contagion, but thinks that the tubercle bacilli is ubiquitous and exists in us all and only awaits suitable conditions to develop.

On page 45 is a statement that tubercle bacilli may in some individuals become modified in some inexplicable manner, *e. g.*, by badly cured fish which may so affect the bacillus within the body that leprosy instead of tuberculosis is the result.

Elsewhere the author suggests that the leprosy bacilli may develop in fish under conditions of decomposition, although such a development may be very exceptional, yet it is always possible.

Hutchinson believes that the disappearance in some places and the marked decrease in others of leprosy during the Middle Ages was due to the spread of Protestantism, which did away with the compulsory eating of fish two days a week.

The author asserts again and again that the disease is not contagious and cites a mass of evidence of various kinds to prove this statement; *e. g.*, there are many scattered lepers living in London, Paris, Vienna, Berlin, and in the United States, yet one never hears of any contagion nor of any epidemic. Cases have been frequently recorded where a husband having leprosy and a wife free of it have lived together for many years without the latter contracting the disease.

In a Madras (India) asylum there were 148 couples where the husband was a leper but the wife not; and in 43 other couples the conditions were reversed, the wife was a leper and the husband not; but all these couples lived together as if both husbands and wives were in good health. Attendants in leper asylums seldom contract the disease.

For many years numbers of lepers, as the author states, emigrated from Norway to the United States, yet no one maintains that the disease has spread in the United States. Hutchinson's thorough investigation of the evidence at hand seems to show that leprosy is not contagious.

In a discussion before a medical society in Cape Colony to a local doctor who said he would never accept the fish theory until the bacillus had been demonstrated as being present in fish, Hutchinson answered, "a blessing was promised to those who could on occasions believe without having seen."

It is rather curious to note that all attempts at inoculation have failed up to the present.

As the result of his "fish theory" the author compares leprosy to chronic ptomaine poisoning.

To sum up, Hutchinson has collected a remarkable amount of direct and indirect evidence which almost convinces the reader that leprosy is due to eating bad fish, although the bacillus of leprosy has never been demonstrated in them. The advice which he therefore urges strongly is, do not eat bad fish or badly-cured fish or you may contract leprosy. This may sound rather ridiculous to the people of the United States, England, Germany, etc., but is very necessary for those who live where leprosy abounds.

Now what are the opposing views to the fish theory? They are: 1. All cases of leprosy cannot be explained in this way. 2. The bacillus of leprosy is found in practically all cases of this disease and yet has never been demonstrated in fish. 3. Recent investigations, by Dr. Goodhue of Hawaii, have shown that bed bugs may be the carriers of the disease, as the bacilli have been found in them and also in mosquitoes; but Dr. Arning, when in the Sandwich Islands, examined mosquitoes after they had bitten the cutaneous lesions of lepers and failed to find the bacilli in them.

When one looks back only a few years and remembers the many divergent views put forward about the cause and transmission of malaria as due to miasmas, telluric influences, etc., and compares them with the present scientific view one cannot but feel that the insect (bed-bug) theory of the transmission of leprosy is more likely to be proved correct than the fish theory.

The book can be highly recommended to those who are at all interested in leprosy.

The Journal of Hygiene. Vol. VI. No. 4. (*Cambridge, England: University Press.*)

This "extra" number of the above-named journal, containing "Reports on Plague Investigations in India," contains ten most valuable and interesting papers, illustrated with a number of plates, by the members of the committee appointed to pursue these studies; the articles consider various questions in relation to plague, as for instance, the transmission of plague by fleas, the species of fleas found upon rats, and the anatomy of the mouth parts and alimentary canal of the Indian rat-flea. There are other reports on the immunity of rats, on the infectivity by floors contaminated by the plague bacillus, on the existence of chronic plague in rats, etc. As is usual in the reports issued by English Government committees the work has been admirably done; the articles, though brief, are clear, well written, and important contributions to the subject of plague, and the complete, for this is but a preliminary report, will be awaited with eagerness. The necessity of such investigations is clear to all; plague is the most dreaded of all diseases in countries where it does not naturally exist, and the means taken by States to prevent its spread at moments when it is feared that even a single case may have entered a town are so expensive and burdensome to all the inhabitants that it is to be hoped that the results of the investigations now being pursued so carefully and thoroughly will help to aid all governments as to the proper methods to be used in guarding against a possible epidemic. R. N.

Conferences on the Moral Philosophy of Medicine. Prepared by an American Physician. (*New York: Rebman Company, 1906.*)

This small volume is entitled on its cloth cover "A Book for Medical Students and Young Practitioners;" but neither title gives a clear idea of its contents. The conferences are intended to serve as a guide to moral conduct for young doctors in all their relations with their patients, "confrères," and the public. Much of the advice given is good, but the work is a pretentious one, and the author has done well not to sign his name to it. It will do no one harm to read it, but it is doubtful how much benefit any reader will derive from it. There are other far better works on this subject. Although the author devotes a couple of chapters to doctors as writers, yet his own style is so bad oftentimes that his example is to be carefully avoided. His sentences are frequently too long, involved, and wrongly punctuated; and he has a bad habit of using too many adjectives. But perhaps his worst fault is in the use of rare words, or new words coined by himself. The following words used by him are not to be found in the Century Dictionary: Physiophist, logophylist (a favorite word of the author's), monstrate, etical, morphism, morphicly, etc. In the case of the last three words he advocates their use, respectively, for eitological, morphology, and morphologically. He says "pathic" or "morbid" should be used rather than pathological; his reason for this is not clear, nor does he explain the difference which he says exists between "autopsy" and "post-mortem examination," nor between "catheterization" and "catheterism," words which, according to the Century Dictionary, are interchangeable. Instead of pathology he says "patho-anatomy," which is certainly a poor substitute. He uses "olfactive" for "olfactory," and "sensual" for "sensuous"—both serious errors; again, "ungrammatic" for "ungrammatical." He speaks of "verbal bankruptcy"—a condition from which he seems to suffer, when he uses the word "macrology." One quotation to close with, and all will have been said that is necessary to convict the author of an uncultured style: "The prudent young scholar will tactfully avoid verbal encounters with the vulgar and never unsheath his intellectual weapons against those gigantic word-mills that perpetually grind out all manner of literary heresies." R. N.

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TO THE MEDICAL PROFESSION OF MARYLAND:

The medical profession of San Francisco lost its medical library, the San Francisco County Medical Society Library, in the fire last spring. Most of the physicians also lost whatever private libraries they had succeeded in collecting. A committee (named below) has been appointed by the American Medical Association and by the Association of American Physicians to collect and send books to San Francisco, both for the library and for private individuals when duplicate copies are sent on, as they are sure to be.

Will you send to Dr. W. S. Thayer, 406 Cathedral Street, Baltimore, Maryland, any medical books of value or bound volumes of journals which you can spare? Fairly recent editions of standard text-books, foreign text-books or bound journals (French, German, and Italian), hospital reports, monographs of all sorts, books on special subjects, old classics, (e. g. Trousseau, Charcot) and the Sydenham Society publications are especially desired.

Acknowledgment of all that is received will be made through the medical journals and the books will be packed and shipped as promptly as possible. Signed,

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TRACHOMA IN THE AMERICAN NEGRO RACE.

By J. Bordley, M. D.

The title of this paper rather implies a belief on my part that the American negro race is subject to, probably the most dreaded of all eye diseases, trachoma. Indeed this paper was written with the idea in mind that such a thing is a mere theory impossible of proof by any existing data. After a careful review of the literature I am not convinced that any case has been recorded of trachoma in the American negro. Indeed not one true bill was found.

Dr. Swan Burnett had the distinction of first calling the attention of the profession to this interesting condition in 1876. Theobald, Hamilton, and many other distinguished oculists have written articles substantiating his views. These men have all enjoyed large experience in the treatment of negroes and the weight of their evidence is very convincing.

In reporting cases of trachoma in the black race unfortunately the essential characteristics of the disease have in the majority of instances been overlooked. It seems totally unnecessary to a few writers that the cases should bear some resemblance, either etiologically, symptomatically, or as regards the sequelæ, to the disease as it occurs in the white race. In determining what trachoma is are we to consider macroscopical signs only? Have we the right to class as trachoma cases which do not originate from contagion, do not follow typical courses and terminate without leaving the signs never absent as a result of trachoma in the white race? I am convinced that many cases are reported as the result of that process of elimination recommended by Peter Shaw, in 1738, when he said, in speaking of treating "Simple Ophthalmia": "Let this be continued according to the indication, and if it happen to be without success call it ophthalmia strumosa and treat it as a strumous case."

Trachoma is an acute contagious disease of the conjunctiva, characterized by the formation of papillary overgrowths or granules, or both, and terminating in the formation of cicatricial bands in the conjunctiva of the lids. One of the striking incidents of the disease is an infection of the cornea as a result of minute abrasions caused by constant friction of the diseased lids over the cornea, this infection is called pannus.

The disease was first given serious attention during the Napoleonic wars; since then the morbid processes of this dread affection have been given more attention than any other single ailment of the eye. From Vescht (1807) to Parsons (1905) the most able workers in ophthalmology have been bending every energy to find the cause of and the cure for trachoma. While the cause is not known beyond the fact that the disease is contagious, Hirshberg and Krause described bacilli in acute but failed to find them in chronic cases; Koch believed the Koch-Weeks bacillus to be a concomitant cause with the gonococcus; Sattler described a small diplococcus as did Michel, Schmidt, Raehlmann, Staderini, and others. The micros-

porum furfur, mixed infections, and plasmodia (of which 62 evolution forms have been described) have each and all at some time occupied the attention of the profession and, by some been regarded as the cause of trachoma. There seems to be but one point in the course of the disease which has been definitely settled and upon which all authorities agree, that is, the existence in the conjunctiva of granules is pathognomonic. The essential feature of all clinical trachoma, whether papillar, granular, or mixed is the trachoma follicle. We often find in the human conjunctiva poorly developed follicles and by such authors as Krause and Baumgarten they are regarded as physiological, Waldeyer and Wolfring, however, take the opposite view, regarding them always as pathological.

While we must undoubtedly agree that granules are never seen in the conjunctiva except as a symptom of trachoma we must not at the same time lose sight of the fact that many of our leading text-books in describing the disease have confused follicles with granules. I have no doubt from the description of some of the reported cases in the negro that the surgeon was dealing with a rather typical case of follicular conjunctivitis and, following the lead of some text-book had confused follicles with granules. While we agree that follicles are necessary to trachoma we consider them in no sense pathognomonic. Even in describing follicles we must bear in mind that other conditions can so closely simulate this condition as to require a microscopical examination to determine the difference. The follicles which are found in trachoma are definite anatomical structures, consisting of "reticular tissue of the adenoid layer of the conjunctiva, lymphoid elements in the meshes of the stroma, vessels which surround and send sparse capillaries into the follicle, and a fibrous tissue capsule." We must follow these follicles from the time they make their appearance to the time of their disappearance. In follicular conjunctivitis they decrease in size as the patient improves, ultimately either disappearing entirely leaving no sequelæ or, as is more common, returning from time to time to start fresh trouble; in trachoma resorption of these follicles may take place at any stage, by mere retrogression without softening, or, as is more usually the case, by degenerative changes which take place in the cells, dependent according to Raehlmann, upon sclerosis of the blood-vessels at the periphery and in the neighboring conjunctiva. No matter which way the disappearance of the follicles is brought about, the space is occupied ultimately by connective tissue. The contraction of this connective tissue always leaves as a permanent mark of former trouble, linear scars.

While I do not say that all the reported cases of trachoma in the American negro are errors in diagnosis still all lack some vital point which I cannot pass over unquestioningly.

It is claimed by Van Milligan that in Turkey the negro is beset by this disease. Fernandez, after an exhaustive study of the subject in Cuba, makes the statement that there the negro enjoys an almost complete immunity. How the American negro gains this immunity is a question yet unsolved. Perhaps, as has been suggested, we should bear in mind the negroes of Turkey may have originally belonged to entirely different tribes, may have been reared under vastly different circumstances from the negroes in America. The possibilities from the introduction of a different strain must not be overlooked. If the American negroes are not immune to this disease they certainly possess the power of keeping it to themselves and the happy faculty of getting well and leaving no trace of the disease in either cornea or lids.

I wish here to report three cases which several of my colleagues as well as myself diagnosticated trachoma. The first was a man, aged 31. He is a typical negro, black, ignorant, and stupid. On applying for treatment he said his right eye—the only one affected—had been "bad" for two weeks, pained him very much and "the lids stuck together every morning." I found the lids swollen and tense, a sero-mucus discharge constantly dripping from between the closed lids, the ocular conjunctiva was œdematous and injected, photophobia was intense, iris clear and pupil normal, cornea clear. On everting the upper lid, which was accomplished with the greatest difficulty, I discovered in the retrotarsal folds and in the conjunctiva of the tarsus many small, nodular masses. These masses were so situated as to be definitely outlined and the epithelium so pushed ahead of them as to form small mound-like projections. The conjunctiva over the upper tarsal cartilage had enlarged papillæ giving the conjunctiva the appearance of soft fine velvet. A most diligent search, which was often repeated, failed to demonstrate any grey, translucent, hemispherical bodies which are pathognomonic of granular trachoma.

A culture taken from the cul-de-sac of the conjunctiva developed the xerosis bacillus; this organism was also cultivated from one of the nodular masses. A section from one of the nodular masses showed only a dense round-cell infiltration of the tissues, there was no attempt at encapsulation and no definite reticular or blood-vessel formation could be described, while the epithelium was more flattened than normal the change was insignificant. Attempts at animal inoculations with a pure culture of the organism were negative.

A 20 per cent solution of protargol was instilled in the eye three times a day as was also a 1 per cent solution of atropine. At the end of two weeks the patient had grown much worse, showing what were considered most definite symptoms of a bad case of trachoma. The trouble was at this time complicated by the formation of three small corneal ulcers. It is not the usual rule to find corneal ulcers in the first stages of trachoma, they most often make their appearance as secondary results in the pannus formation. Up to this time our treatment was without avail, suddenly, however, during the

seventh week the eye began to improve and at the expiration of nine weeks the patient was discharged, cured.

Case No. 2 was also a negro man, about 31. He was rather more intelligent than the one to whom I have just referred. His right eye "had been sore" for forty-eight hours before applying for treatment, the lids of the affected eye were so swollen and tense that I could not evert the upper lid or see the retrotarsal fold in the lower lid, the eye was injected and the bulbar conjunctiva very œdematous, cornea and iris clear, and pupil normal. There was a profuse sero-mucus discharge, great pain, and photophobia. I strongly suspected at the beginning a gonococcus infection of the conjunctiva, although the history was absolutely negative and no gonococci were found microscopically.

The case was put on active treatment and placed in the hospital. The treatment consisted of ice-pads, a 40 per cent solution of protargol, and cleansing of the lids as often as was found necessary. The eye responded beautifully to treatment and in a week's time it was possible to evert the lids. In the retro-tarsal folds of the upper lid and over a portion of the tarsal conjunctiva I found the mucus membrane studded with small mound-like projections and the tarsal conjunctiva covered with a velvety papillary structure. A culture taken from the secretion in the retro-tarsal fold developed a pure culture of the Xerosis bacillus. A slide taken from the same secretion showed short, thick bacilli. I regret to say the patient would not allow me to remove any of the conjunctiva, consequently I was unable to study what I believed to be follicular enlargements. Animal inoculations with a pure culture of the organisms were negative.

Two small corneal ulcers made their appearance during the fourth week of the disease. These ulcers disappeared as the lid conditions cleared up. The patient was discharged, cured, nine weeks after the first symptoms had made their appearance.

Case No. 3 differed from the two preceding cases in only two ways: first, both eyes were infected; second, three small tarsal cysts developed in a short time after the case had been discharged. A culture taken from the secretion, developed xerosis bacilli. Sections from nodules showed only the signs of a non-purulent inflammation of the conjunctiva. A slide taken from the contents of one of the chalazia, which were subsequently opened, showed no bacteria. The nodular masses in the conjunctiva, the papillary enlargements in the tarsal conjunctiva, and all the acute symptoms were present in this case as in the others.

I believe no man could have drawn any other conclusion from watching the first symptoms of these three cases than that they were trachoma. Still, now that the cases are well and we sum up the evidence to complete our diagnosis, we must grant that our original observations were based on false premises.

To sum up we found these symptoms which were identical with those of trachoma: a sudden onset, swelling of the lids, a sero-mucus discharge, œdema of the bulbar conjunctiva, apparent follicular enlargements in the palpebral, and papillary overgrowths on the tarsal conjunctiva, pain and photophobia, and the obstinacy of the disease in spite of active antiseptic treatment. Several features necessary to complete a diagnosis of trachoma were, however, absent: no hemispherical, granular bodies were to be discovered in the retro-tarsal folds; the cases did ultimately get entirely well, leaving no scar tissue as a result of the conjunctival trouble; at no time, either during or subsequent to the disease, did a pannus make its appearance; in two cases one eye also was infected; two of the patients were in institutions and frequently, in spite of my advice to the contrary, used towels in common with other people, still, so far as I can find out, no one was infected. I think if we add to these facts the additional evidence that the xerosis bacillus was developed in pure culture in every case and that a histological examination of the supposed follicles in two cases showed only the signs of an acute, non-purulent infection of the conjunctiva with no definite body arrangement such as is found always in trachoma, we can conclude that we were not dealing with trachoma.

Not taking into consideration the bacteriological and pathological findings in these cases does not the evidence seem to indicate that we were not dealing with trachoma? Parsons says that follicles always go on to cicatrization and that trachoma can not exist without the formation in the adenoid layer of the conjunctiva of follicles. Burnett says the only positive evidence of trachoma is the formation of scar tissue in the conjunctiva; Raehlmann coincides with this view and so do all the other authorities on trachoma. These cases of mine show no evidence of scar tissue and never did. Trachoma in the white race is violently epidemic; still two of these cases I report lived in institutions where people were crowded together, and used in common with many others roller towels and yet not another case developed. Trachoma nearly always attacks both eyes: two out of three of my cases had trouble with only one eye. Pannus is nearly always a sequel or an accompaniment of trachoma; then why was it, if my cases were trachoma, not one of them showed the slightest sign of corneal trouble beyond the small ulcers and the scars resulting from them.

I must conclude that under certain circumstances the xerosis bacillus attacks the conjunctiva of the negro and provokes an inflammation which so closely simulates trachoma as to make it impossible in the first stages to make a certain diagnosis. There is this essential difference, however, the inflammation resulting from the xerosis infection gets well and leaves behind it no traces of the active conjunctival trouble. I can readily imagine this difference not holding good if a secondary infection of the conjunctival nodules by a pyogenic organism should take place, for surely then the sloughing ulcers would result in the formation of cicatrices.

The only evidence adduced to prove the disease is caused by the xerosis bacillus is the fact that cultures taken from the secretions and the nodular masses developed the bacillus in pure culture. Animal inoculations were negative.

I wish to thank Dr. J. M. Love for the valuable assistance rendered me in working out the bacteriology of this disease.

A REPORT OF FOUR CASES OF MEMBRANOUS DYSMENORRHEA.

By Elizabeth Morse, M. D.

The term "membranous dysmenorrhea" is applied to cases in which considerable portions of the endometrium are thrown off repeatedly at the menstrual period, usually with pains simulating those of labor. The cases vary in severity from the typical form in which a complete cast of the uterine cavity is discharged at each period with great pain, to the milder ones in which small fragments of the endometrium are passed with only slight symptoms at intervals of several months. Painless cases have occasionally been reported. The passage of a single membrane from the uterus does not constitute a case of membranous dysmenorrhea.

The affection is not a disease *sui generis;* but a condition which develops under varying circumstances, complicates different pathological processes, and presents a variety of microscopic appearances. Some writers have, therefore, suggested that the purely clinical term "membranous dysmenorrhea" be abandoned, and "exfoliative endometritis" (Wyder) (9), or "exfoliation of the menstrual mucosa" (Löhlein) (17) be substituted.

The etiology and pathogenesis of the condition are obscure, and the treatment has been attended with little success. This is due partly to the fact that the affection is in reality rare, and the specimens available for study still more infrequent. The milder cases are often not brought to the physician's attention, while, on the other hand, the diagnosis is frequently made on insufficient clinical data, and without a microscopic examination of the membrane. The latter point is illustrated by the fact that, of eleven specimens sent to the gynecological laboratory of the Johns Hopkins Hospital with the diagnosis of "membranous dysmenorrhea," only three proved, after investigation of the patients' history and examination of the membrane, to be genuine cases. The other specimens showed decidua in four instances, vaginal epithelium in two, and one example respectively of uterine polyp and blood-clot.

The disease was first recognized by Morgagni (1), who reported a case and gave an excellent description of its clinical course. Denman in 1791, also described membranes, but thought them identical with decidual casts, previously described by Hunter. The first microscopic study of menstrual membranes was made in 1842 by Ernst Heinrich Weber, and the term "membranous dysmenorrhea" was applied to the condition by Oldham and Simpson in 1846 (2). A certain resemblance to decidual tissue impressed observers more and more strongly, so that a prolonged discussion was carried on, especially in Germany, as to whether all cases of membranous dysmenorrhea were not in reality merely repeated early abortions. Only within the last thirty years have the two conditions been clearly differentiated. The first adequate histological study in the modern literature on the subject is that by Wyder (1878) (9). Von Franqué, in 1893 (23), reported five cases and made an elaborate study of the pathological anatomy. Since his article numerous isolated cases have been reported, but little new information has been added to the subject.

The most important etiological factor in the condition is a preceding endometritis, arising after child-birth, an abortion or a gonorrheal infection. In other instances there is a retroflexion or some abnormality of the appendages. A considerable number of cases, however, occur in young unmarried women, with no history of infection and with pelvic organs apparently normal on examination. There is in this group, of course, the possibility of an overlooked vaginitis in childhood, or an endometritis accompanying the exanthemata.

The clinical history is usually somewhat as follows: Menstruation was regular and normal until after a labor or an abortion followed by fever, or after a gonorrheal infection. Dysmenorrhea then developed, followed in a few months by the appearance of membranes. These may be discharged only at intervals of three or four months. Usually, however, one is passed at each period; in exceptional cases two or more. Menstruation is accompanied by pain, and the expulsion of the membrane, which usually occurs on the third or fourth day, is preceded by intermittent uterine contractions, similar to those of labor. These cease after the discharge of the membrane, which is often followed by copious hemorrhage.

The prognosis as to recovery, either with or without treatment, is not good, as the condition usually persists until the menopause. Sterility is the rule, although a few patients recover and become pregnant.

The treatment most often adopted in cases where the underlying condition is obscure, is curetting a few days before menstruation, followed by the application of tincture of iodine or carbolic acid to the uterine cavity. This procedure frequently gives temporary relief, but the patients usually relapse within a few months. Any associated lesions of the uterus or appendages should of course receive appropriate treatment.

The menstrual membrane, when discharged entire, forms a triangular sac, having the shape of the uterine cavity, and sometimes showing rounded holes at the sites of the tubal openings. The outer surface (*i. e.,* towards the uterine wall) is ragged; the inner is smooth. The thickness of the membrane varies from that of tissue paper to two or three millimeters. Membranes of greater thickness suggest decidua. Complete casts of the uterine cavity are rarer in membranous dysmenorrhea than in pregnancy, the tissue in the former condition being usually passed in fragments.

A variety of microscopic appearances have been described in this condition. The membranous discharges from the uterus may be divided, however, into two groups (excluding decidua for the present): exfoliated mucosa and fibrinous casts.

In membranes composed of altered mucosa, two pictures

may be differentiated in a general way. The first is that of an interstitial endometritis. The stroma cells are of normal size and appearance, and there is an infiltration of lymphocytes. Hemorrhage, exudate, and fibrin are usually present in addition. In the second type the stroma cells show a strong resemblance to decidua. They are enlarged, oval or polygonal in shape, with a large vesicular nucleus and abundant protoplasm. All gradations may be traced between these decidua-like forms and the normal stroma cells. The entire membrane may be composed of these altered cells, or glands may also be present. Occasionally a compact and a spongy layer can be distinguished. The two pictures—interstitial endometritis and decidua-like areas—are often seen in the same membrane. It is these enlarged stroma cells which have given rise to so much confusion and to a prolonged discussion as to whether there is any criterion by which they may be differentiated from true decidual cells. They are usually interpreted in menstrual membranes, as the result of chronic hyperæmia and irritation. They are not, however, peculiar to this condition, being found also in glandular hypertrophy and œdema of the endometrium, where they are accounted for by circulatory changes.

Most membranes show signs of degeneration, varying from a hydropic appearance of the cells and inability to take ordinary stains, to coagulation necrosis. A "budding" of the interglandular tissue has been described by Von Franqué (23) and also by Hegar and Maier; *i. e.,* compact foci of stroma cells in which growth is more active, and which penetrate independently in different directions through the loose stroma. These authors found them also in the hyperplasia of the decidua associated with hydrorrhea gravidarum. They consider it a change which may be found in any plastic inflammation.

Amyloid change in the vessel walls has been found in membranes from a case of prolonged and severe pelvic inflammation. Large numbers of eosinophiles and also mitoses in the stroma cells have been reported by several observers.

Fibrinous casts are composed of a network of fibrin containing in its meshes red corpuscles, leucocytes, and remnants of the cells of the mucosa. There is some doubt as to whether these casts should be classified with true cases of membranous dysmenorrhea. Some authors exclude them entirely. They develop, nevertheless, in connection with endometric processes, and are passed with the same symptoms as the organized membranes. In fact, cases have been reported, in which the same patient passed at one time a fibrinous cast, and at another a membrane of altered mucosa. It is impossible, also, to separate the two varieties anatomically, as many transitional forms are found between the simple fibrinous cast and the well-preserved, exfoliated endometrium. Schönheimer (22) considers the process to be an acute fibrinous inflammation occurring under the influence of menstrual congestion, after a terminated endometritis, and subsiding at the end of the period.

The mechanism of separation of the membrane is obscure. The most generally accepted theory is that the hyperplasia of the stroma cells causes an obstruction to the escape of blood into the superficial layers; hence it spreads out in the deeper portions of the mucosa. The tissue, friable because of chronic hyperæmia and its young connective-tissue cells, yields in its weakest part, and the membrane is dissected off by hemorrhage. The free bleeding which frequently follows the expulsion of the cast is thought to confirm this theory. An abnormal density in the superficial layers of the endometrium would also hinder the escape of the blood, and lead to the same result. Speaking against this mechanical theory of separation is the fact that the blood is often distributed equally through all parts of the membrane.

The degenerative changes found in the greater number of membranes must also be an important factor in causing separation,—possibly quite as important as they are in the separation of the decidua. Regressive processes in the decidua—chiefly coagulation necrosis with the appearance of fibrin—appear in the second half of pregnancy and are marked at term. The membranes from our first case show widespread coagulation necrosis in the stroma, and in the second case the process is beginning. In both cases there are pronounced changes in the blood-vessels,—many are occluded with fibrin and their walls degenerated.

The diagnosis of membranous dysmenorrhea, although it may be very probable from the clinical history, should not be made without a microscopic examination, as there are two other discharges from the genital tract, which may simulate menstrual membranes macroscopically. These are vaginal casts, or fragments of vaginal epithelium, and decidual casts. The former are thrown off, either as the result of an exfoliative vaginitis, or treatment of the vagina with strong chemicals, such as silver nitrate. The tissue in exfoliative vaginitis may be passed either during menstruation or independently of it. If the pieces are passed with pain during the period, the case may be considered one of membranous dysmenorrhea. This was the case in two specimens sent to the laboratory, with the diagnosis of "membranous dysmenorrhea," and proving, on microscopic examination to be of vaginal origin. An exfoliative vaginitis may accompany a true membranous dysmenorrhea. Leopold (11) reports a case of this kind, and considers the cause of the two processes the same, *i. e.,* a superficial hemorrhage, arising from extreme hyperæmia, and extending through the cervix into the vagina. Hoggan (6) describes a membrane, the upper part of which was composed of uterine mucosa, the lower of vaginal epithelium. If small portions of vaginal epithelium are passed together with endometrium, the former may be overlooked, in case only the larger pieces in the specimen are examined.

As a rule vaginal casts and pieces of vaginal tissue are thinner, tougher, and more parchment-like than membranes from the uterus, and no glandular openings are seen on the surface. The diagnosis can be made immediately with the microscope.

Decidual casts are expelled in abortion, extra-uterine pregnancy, and in the rare cases of pregnancy in one horn of a double uterus. The typical decidual cast is larger, thicker,

and more vascular than the dysmenorrheic membrane. If chorionic villi are found on microscopic examination, the diagnosis of intra-uterine pregnancy is of course clear. If decidua alone is present, the only diagnosis that can be made, from consideration merely of the cast, is that of the existence of pregnancy,—either in a normal uterus, a rudimentary horn, or a tube.

The greatest difficulty, however, has arisen over the differential diagnosis of an early abortion from a menstrual membrane containing large decidua-like cells. The question arises chiefly in cases of early pregnancy, before the decidua has reached its full development and typical form. Cells, which in size, form, nucleus, and staining properties closely resemble true decidual cells are found apart from pregnancy, not only in menstrual membranes, but also in œdema of the endometrium, glandular hypertrophy, and inflammatory conditions of the mucosa. There may be no difference in size between these enlarged forms and decidual cells, as was proved by Von Franqué (23) in a series of measurements; but the former do not show the epithelioid appearance found so often in the mature decidual cell, which has more abundant protoplasm and a much more sharply-defined outline. The protoplasm of the decidual cell also loses its fibrillated appearance and takes a deeper eosin stain. Although the differential diagnosis of a menstrual membrane from typical decidua is usually clear on microscopic examination, there are many confusing cases, in which the question of early pregnancy cannot be excluded without the aid of the clinical history.

There are specimens from three cases of genuine membranous dysmenorrhea in the collection of the gynecological laboratory of the Johns Hopkins Hospital, and also one specimen of a fibrinous cast, which, from the patient's history, should be included in this group.

The cases are as follows:

Case I.—L. R., age 20. Gynecological history No. 12,427. Sent by Dr. G. K. Vanderslice, Phoebus, Va. Was admitted to the Johns Hopkins Hospital, October 11, 1905, and discharged October 20, 1905.

Complaint.—Pain in left side, painful menstruation and backache.

The family history was unimportant.

Past history and present illness.—Patient has always been well, aside from the present trouble. There is no history of severe infectious diseases.

Had a tumor removed from the right breast in 1904. Menstruation began at twelve years, is regular every four weeks, lasting seven days, and has been painful and profuse from the beginning. Ever since the onset, so far as patient can remember, she has passed with each period "pieces of flesh." Dysmenorrhea is severe on the first day, less on the second, and on the third day the membrane is passed during a paroxysm of pain, lasting about one hour. This pain, which is always located a little to the left of the mid line, is sharp, and, as patient expresses it, "feels like raking over a raw surface." It is relieved immediately by expulsion of the membrane, which is sometimes followed by considerable hemorrhage; at other times none.

Patient has also less marked paroxysms of pain in the intermenstrual interval. These attacks last frequently but a few minutes, and may occur several times a day, or at intervals of several days. The pain is located in the same spot as during menstruation. Patient thinks that the pieces of membrane passed at present are smaller than formerly, and that she is gradually improving.

About a year before admission patient noticed that the uterus was situated low down, and since then she has been troubled with backache and leucorrhea.

Physical examination on entrance showed a well-nourished girl. The heart, lungs, and abdomen were normal.

Pelvic examination under ether gave the following: Outlet, virginal; no signs of infection; cervix low, 1½ in. from the outlet; fundus in anteposition; freely movable; both ovaries easily felt and apparently normal.

A dilatation and curetting were performed, and a very small amount of endometrium, normal in appearance, was obtained (nineteen days after the last period). The specimen unfortunately was not saved.

Patient made an uneventful recovery, and was discharged ten days after admission. She sent to the laboratory some material passed during the period in November, which on microscopic examination showed nothing but blood clot.[1]

The laboratory possesses three specimens from this patient, the first passed when she was fifteen years old, the second in August, 1902, at the age of seventeen, and the last in March, 1905. There is a certain similarity in the membranes, all of which show marked vascular, inflammatory and degenerative changes, and the first two also glandular hypertrophy.

The first membrane (gyn. path. No. 8315), has been imperfectly preserved and stains poorly. Surface epithelium is absent. The glands, which run parallel to the surface, are irregularly distributed. In the upper half of the membrane they are scarce, and lacking altogether in large areas. In the lower part of the membrane, however, they are increased in number, and in some places form a tortuous mass, separated by only scanty stroma. The epithelium is sometimes reduplicated and projects into the lumen in the form of tufts. The dilated lumina contain desquamated epithelium; red corpuscles and fibrin.

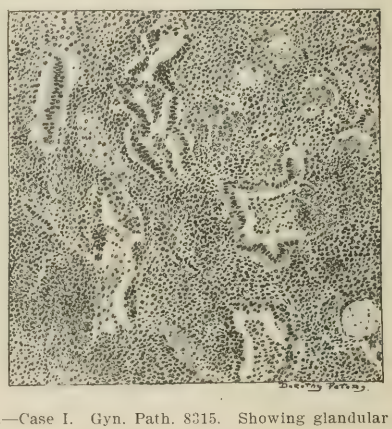

Fig. 1.—Case I. Gyn. Path. 8315. Showing glandular changes and areas of beginning necrosis in stroma.

The stroma cells are not increased in size, and aside from a degenerated appearance, due partially to the poor preservation, show no abnormality. Small areas of beginning necrosis, from which networks of fibrin radiate, are scattered through the

[1] A letter from patient's physician dated April 15, 1906, states that she is again passing membranes, but with less pain.

stroma. The blood-vessels are numerous and comparatively large. Some are filled with well preserved red corpuscles; others with fibrin. Shadows of red cells are found throughout the tissue; also numerous leukocytes.

The membrane passed in August, 1902 (gyn. path. No. 8399), consists of a piece of tissue about 3 mm. thick, and approximately the size and shape of the uterine cavity. Microscopically it presents a striking picture, on account of the marked glandular hypertrophy and the extensive degenerative changes.

FIG. 2.

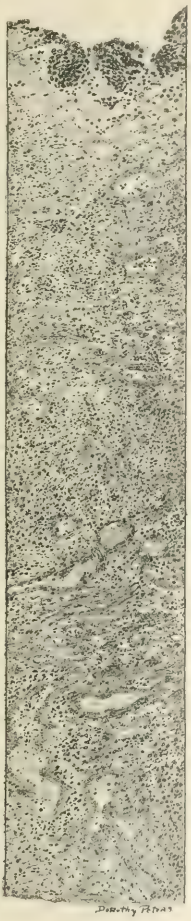

FIG. 3.

FIG. 2.—Case I. Gyn. Path. 8399. Section through entire thickness of membrane, showing glandular dilatation, changes in blood vessels and degeneration in stroma.

FIG. 3.—Case I. Gyn. Path. 8400. Section through entire thickness of membrane, showing extensive necrosis and changes in blood vessels.

The surface epithelium is mostly lacking, being represented only by a few groups of cuboidal cells. The stroma immediately beneath the surface is thickened, and contains compressed and atrophied glands, which run parallel to the surface. In the deeper portions of the membrane are groups of tortuous and greatly dilated glands. They are lined with a single layer of low-cylindrical epithelium, and their lumina are filled with fibrin, red cells and leukocytes. In the neighborhood of these glands are numerous very large thin-walled vessels distended with blood. The stroma cells are somewhat enlarged. In a few areas near the large blood-vessels they stain clearly. For the most part, however, the cell outline and nucleus are indistinct and stain faintly and diffusely. Many of the cells are swollen. Some nuclei are shrunken and take an intense stain; others are undergoing fragmentation. The stroma cells are widely separated by fresh hemorrhage and exudate, and there is everywhere an abundant network of fibrin and a thick infiltration with polymorphonuclear leucocytes. The blood-vessels are numerous and large. Many are filled with fibrin and the walls of some of the smaller stain homogeneously with eosin, as if undergoing hyaline change.

The membrane expelled in March, 1905 (gyn. path. No. 8400), shows more advanced degenerative changes than the preceding. It is composed of thickened stroma, showing areas of coagulation necrosis, especially in the region of the blood-vessels. Clinging to the edges of the membrane are fragments of well preserved glands and stroma. The cells of the membrane are somewhat larger than normal. They all stain diffusely, are indistinct in outline, and show shrinking or fragmentation of their nuclei. The blood-vessels, which are numerous in the deeper portions of the tissue, show marked degeneration, their walls stain homogeneously with eosin, and their lumina are filled with fibrin. The entire membrane is traversed with a network of fibrin and thickly infiltrated with polymorphonuclear leukocytes.

CASE II.—The membrane from this case was sent to the laboratory February 7, 1905, by Dr. J. B. Beeson, of Livingston, Montana, with the following history: The patient, age 30, is a well-formed, healthy-appearing woman, married five years. Her menstrual history was normal until the appearance of the membranes. She had one or two abortions (probably artificially induced), during her early married life; for the past two or three years, she has not been pregnant. She began to pass membranes eight or nine months ago, and since then has discharged one at each period. Severe dysmenorrhea, confining her to bed for two or three days, developed coincidently with the appearance of the membranes. No pelvic examination was made and the patient has been lost sight of.

The specimen (gyn. path. No. 8239), consists of a few shreds of grayish-red tissue. Microscopically it is composed almost entirely of stroma. The surface epithelium is absent, and only an occasional remnant of a gland is seen. The stroma varies much in density; the cells in some areas being more closely set than normal; in others separated by exudate and their character changed. The rarified areas are, as a general rule, near the free surface of the membrane; the denser areas in the interior, where they occasionally surround the blood-vessels. The largest of the altered stroma cells have round, vesicular, faintly staining nuclei, two or three times the size of those of the usual stroma cells. The cell outline cannot be defined; but the protoplasm is small in amount and stains very faintly with eosin. Every gradation can be traced between them and the normal stroma cell. Numerous thin-walled vessels are present throughout the section, most of them occluded with fibrin. From them a delicate network of fibrin spreads out into the surrounding tissue. Indeed, the abundance of fibrin, both within and without the vessels is a striking feature. Scattered everywhere throughout the membrane are foci, in which the fibrinous network and the leucocyte infiltration are denser, and the stroma cells are indistinct and stain diffusely. In a few

places the process has advanced to actual necrosis. There is everywhere a marked infiltration with small round cells, especially about the thrombosed vessels.

Even in the absence of a pelvic examination, both the clinical history and microscopic appearance of the membrane point to an inflammatory origin in this case.

Case III.—The following history is obtained from Dr. C. D. McLeod, of Chatfield, Ohio, who sent the specimen to the laboratory. The patient, age 38, was married at 16 years of age, and has four children. No history of puerperal infection. She has had marked dysmenorrhea for the past seven years, and during the last two or three years has passed shreds of membrane. She has also been subject to severe pain in the pelvis about ten days after menstruation. About twelve years ago she had some nervous trouble, diagnosed as "cerebro-spinal meningitis," which has left her with a partial paralysis of the left side.

Fig. 4.—Case III. Gyn. Path. 8648. Showing enlarged stroma cells. (Drawn by Miss Young.)

The physician when called to the patient in November, 1904, found her having alarming hemorrhage and severe intermittent pains. He removed a complete cast of the uterus (the present specimen), which he took at the time to be an abortion sac. Pelvic examination showed a prolapsed, enlarged and softened uterus. The two periods following this one were also attended by profuse hemorrhage. The patient then improved temporarily, and would pass two or three periods without discharging membranes. She has relapsed since, however, and membranes have again appeared.

The specimen (gyn. path. No. 8648), is composed of the upper portion of the endometrium, about 1 mm. in thickness, and gives the impression of having been separated en masse. The appearance is perhaps due partially to the fact that manual aid was given in the removal of the cast. The inner surface is smooth and the epithelium fairly well preserved. The surface towards the uterine wall is ragged and shows parts of glands, some of them abruptly torn across, projecting beyond the stroma. The glands are convoluted and dilated. Their epithelium shows no abnormality. The stroma is denser towards the surface; in the lower layers separated by exudate. The cells are considerably enlarged, oval or stellate in outline, and have a round, pale-staining nucleus and an increased amount of protoplasm. Many have a swollen and hydropic appearance. They are pushed apart by serous exudate and in some areas by a small amount of hemorrhage. Numerous lymphocytes are scattered everywhere throughout the membrane. The blood-vessels are abundant, and are filled with well-preserved red cells. The degenerative changes and fibrin, so conspicuous in the other membranes, are absent in this specimen.

Fig. 5.—Case IV. Gyn. Path. 8470. Section through fibrinous cast from uterus.

Case IV.—There is in the gynecological laboratory only one example of fibrinous cast of the uterus. This was sent by Dr. E. C. Seufert, of Chicago, with the following history: M. S., single, age 24. Born in Poland and came to America at the age of 18. Has worked in tailor-shops for the past five years.

Had diphtheria and scarlet fever at about eight years of age, with perfect recovery from both. She was very stout at the time of puberty. Menstruation began at thirteen and was irregular for several years. The flow has been slight, lasting for three days, and from the onset accompanied by dysmenorrhea. The pain has increased in severity, and on the third or fourth day of each period during the last three years she has passed stringy mucous and shreds of membrane. No leucorrhea.

Patient consulted the physician in January, 1905, for the increasing dysmenorrhea. She brought with her a complete fibrinous cast of the uterus,—the first one which had been expelled entire.

Physical examination at that time showed the patient to be well-nourished, and the chest and abdomen negative. The uterus was normal in size and position, and movable. Patient refused the treatment recommended, and it has been impossible to trace her subsequent history.

The specimen from the cast (gyn. path. No. 8470), shows mi-

croscopically a heavy, loose-meshed network of fibrin, in which remnants of cells are in places visible. There is a wide band of fibrin on the surface; below that a layer of finer network; and in the lowest stratum are numerous rounded openings, some of which are artefacts, and others of which seem to have been blood-vessels. The cells which are scattered throughout the network are so degenerated that no idea of their nature can be obtained.

In conclusion I must express my gratitude to Dr. Howard Kelly, who suggested the subject for this paper; to Dr. Elizabeth Hurdon for her constant help and interest; to Mr. Max Broedel for superintending the illustrations; and to the physicians in charge of the cases for their courteous and detailed replies to numerous letters.

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THE MEDICAL LIFE OF OLIVER WENDELL HOLMES.[1]

By J. H. Mason Knox, Jr., M. D.

The birth of Oliver Wendell Holmes into the medical world was hardly a spontaneous one, but was rather the result of a protracted labor and took place after a long period of uncertainty and doubt.

At the age of nineteen, when a junior at Harvard, he writes to his boyhood's friend, Phineas Barnes, that he is totally undecided what to study; "it will be law or Physic, for I cannot say that I think the trade of authorship adapted to this meridian."

While at college Holmes showed in formation many of the convivial charms that so graced his later life. He was popular, the center of much of the social life of his class, and was often called upon at various society and class functions to exercise his ready rhyming pen in descriptive verse. He contributed several articles to the college magazine, the "Collegian." It was here he suffered, as he said, his first attack of "author's lead poisoning."

His father, a clergyman of rather liberal views and latitude for that period seems to have interposed no serious objections to the moderate indulgence of his son's convivial proclivities.

His mother was Sarah Wendell, a sprightly and lovable woman, from whom Holmes inherited many of his genial traits.

He describes himself at college as a "plumeless biped of exactly five feet three inches when standing in a pair of substantial shoes, having eyes which I call blue." "I am rather lazy than otherwise, and certainly do not study as hard as I ought to. I am not dissipated and I am not sedate. I stood at the humble rank of 17th scholar." He graduated in June, 1829, in a class noted for its high character, and which then and for many years afterwards made Holmes the center of their yearly reunions, which he often celebrated in verse.

After this came the well-known period of doubt as to his work. He studied law for a year, but never seems to have liked it. We find him writing in a few months to a friend: "I am sick at heart of this place (the law school) and at almost everything connected with it. I know not what the temple of the law may be to those who have entered it, but to me it seems very cold and cheerless about the threshold."

So after the first year he entered the Harvard Medical

[1] Much of material for this sketch was obtained from the "Life and Letters of Oliver Wendell Holmes," edited by John T. Morse, Jr., 1896.

School September 30, 1830, at the age of twenty-one, and began the studies which brought him contentment and influenced all his later life. He writes to Barnes shortly after his "flop" to medicine: "I must announce to you the startling proposition that I have been a medical student for more than six months and am sitting with a stethoscope on my desk and the blood-stained implements of my profession about me. I know I might have made an indifferent lawyer; I think I may make a tolerable physician. I did not like the one, I do like the other, and so you must know that I have been going to the Massachusetts General Hospital and slicing and slivering carcasses of better men and women than I ever was or am like to be. It is a sin for a puny little fellow like me to mutilate one of your six-foot men as if he were a sheep, but 'vive la science.'"

Little is recorded of Holmes' life at the medical school. Undoubtedly he soon came under the influence of that great clinician and teacher, Dr. James Jackson, who was Professor of the Theory and Practice of Medicine from 1812-1846, and whose son was but a little further on in his medical studies. Dr. Jackson had studied in England and knew the value of the wider experience at the European clinics, and it may well have been at his suggestion that Holmes decided to go abroad and continue his medical education in Paris, which at that time and for a quarter of a century afterwards was the Mecca which all ambitious followers of the healing art sought to reach.

This French nursing converted the weak and underfed medical infant, whose birth had been attended with so many fears, into a sturdy, self-reliant child, able to sit up and take the strong diet of the many clinics and to do some vigorous, independent thinking.

Holmes was associated with a distinguished group of American students, among whom may be mentioned Jackson and Bigelow, Hooper, Warren, Gerhardt, and Morse. They lived in the Latin Quarter and attended the lectures and demonstrations of such men as Louis and Andral, Dupuytren and Larry, who were leading the medical world of their day.

Holmes reached Paris April, 1833, and soon after was completely absorbed in his work. After a few months he writes: "I am more and more attached to the study of my profession and more and more determined to do what I can to give to my own country one citizen among others who has profited somewhat by the advantages offered him in Europe. The whole walls of the Ecole de Médecine are covered with notes of lectures, the greater part of them gratuitous. . . . The dissecting rooms are open and the lessons are ringing aloud through all the great hospitals."

He usually began the day at seven o'clock at the hospital of La Pitié, where he attended lectures and clinics until breakfast at about eleven, after which he studied until 5 p. m., when he often dined at some "café" with a company of his fellow students. He speaks approvingly of the tasteful viands and the pleasing wines, very different from the "crude joints, the massive puddings, the depressing pies, and the hard cider which marvelously nourished New England in its era of development."

The period spent by Holmes in Paris was part of an epoch of remarkable progress in the history of medicine. The short but brilliant researches of Bichat had shown the close relationship between symptoms of disease and definite anatomical conditions and had dissipated many of the philosophical and visionary theories which had been thought sufficient to explain the phenomena of illness.

Following this with the work of Corvesart and Laennec, came the introduction of accurate methods of diagnosis by percussion and auscultation and the insistance by Louis of the statistical method of study; that deductions concerning a diseased state should be made only after carefully tabulating many similar conditions and not from a single instance.

This great teacher, who was just in his prime while Holmes was in Paris, was undoubtedly the most inspiring personality felt by the large group of American students. "Louis had," he writes, "in a rare degree the power of attracting youth, so that those who followed him among the beds of the hospitals became filled with an ardent ambition. He was the object of our reverence, I might almost say of idolatry; modest in the presence of nature, fearless in the face of authority, unwearying in the pursuit of truth, he was a man whom any student might be happy and proud to claim as his teacher and friend." Holmes, apparently was admitted, at least during his second year, to some degree of intimacy with Louis. He writes that he had constant access to two wards containing one hundred beds where he can examine patients and that on one occasion at least he had a "tête-à-tête dinner with his great teacher who intrusted to him the analysis of a work which he is going to make use of in a publication."

He became a member of the Society of Medical Observation, of which Louis was perpetual president and which was devoted to the discussion of important cases and the presentation of new work.

Other luminaries whose path he crossed during the precious time abroad he mentions, particularly in his delightful valedictory address to his class at the Harvard Medical School.

He did not have much to do with Andral who, although then a young man, was rapidly rising in fame and overshadowing the passing greatness of Broussais, whose "theories of gastro-enteritis as the cause of disease ran over the field of medicine like flame over the grass of a prairie, and who was in those days like an old volcano which has pretty nearly used up its fire and brimstone but is still boiling and bubbling in its interior and now and then sends up a spirit of lava and a volley of pebbles."

Of the intrepid men who operated in Paris in those anaesthetic days, Holmes recalled particularly Lisfranc, whom he describes as a "great drawer of blood and hewer of members and who regretted the splendid guardsmen of the old Empire because they had such magnificent thighs to amputate."

Then there was the short, square, substantial man with iron-grey hair, ruddy face, and white apron. This was Baron Larry, Napoleon's favorite surgeon. He was still strong and

sturdy; he adds, "few portraits remain printed in livlier colors on my memory." "To go around the Hôtel des Invalides with Larry was to live over again the Campaigns of Napoleon, to the last charge of the Red Lancers in the redder field of Waterloo."

He visited frequently l'Hôtel Dieu, where ruled and reigned the Master Surgeon of his day, the illustrious Baron Dupuytren. "No man disputed his reign, some envied his supremacy. He marched through the wards like a lessor kind of deity."

He mentions also the vivacious Ricord, whom he called the "Voltaire of Pelvic literature; a skeptic as to the morality of the race in general, who would have submitted Diana to treatment with his mineral specifics and ordered a course of blue pills for the vestal virgins."

His time was not spent altogether in work, for he speaks of quite a list of renowned actors and singers and dancers who contributed to his recreation. He delighted to roam about the streets of Paris at night in looking at the shops which he thinks "greatly superior to those of Boston." He took especial pleasure in hunting for old books on the walls of the "Quais" and at the small dealers. He was present at the dinner among the Americans on July 4, 1833, which was also graced by "that inextinguishable old gentleman, Lafayette."

He was in a dreadful state of anxiety lest he should have to come home after his first year. He seems to have been a considerable drain upon the resources of his good parents, as Holmes, although not extravagant, was not willing to live meanly. He was known as a good dresser. He would come home if he must but he was "not willing to eat a dinner for twenty-five sous and drink sour wine at a cheap restaurant."

However, after several importunate letters he persuaded his father that a "boy is worth his manure as well as a potato patch" and embarked on his second year's work with renewed energy.

In the spring of his second year, with a Swiss who had known successively Jackson and Bowditch, Holmes took a course in operative surgery at a morgue in connection with a large cemetery. "Here at 12 noon every day," he narrates, "you might have seen M. Bizot and myself, like the old gentlemen at market, choosing our day's provisions with the same epicurean nicety. We paid fifty sous a piece for our subject and before evening we had him cut into inch pieces." "In England and America," he says, in contrast, "one may dissect but rarely operate upon the subject."

Holmes spent the summers, after the close of the lectures, in travel. In 1834, with several companions, he visited the Rhine Provinces, the low countries, and England. In London he saw something of the hospitals, but was not weaned from Paris as the city of his choice.

In July, 1835, he packed his accumulated belongings, a select little professional library, a modest stock of instruments, two skeletons and some skulls, and in the autumn, after an extended tour in Switzerland and Italy, he returned home, landing in New York in December. I have dwelt, perhaps, unduly upon the foreign experiences of Dr. Holmes, but it seems to have exerted a controlling influence upon all his subsequent professional life.

He returned to America with high ideals, with well-developed powers, a large amount of professional knowledge and skill, a self-reliance, an independence of thought, and a store of pleasant and useful memories which formed a part of his life's equipment through all the succeeding years.

In 1836 he took his degree of Doctor of Medicine from Harvard University and immediately started to practice. He shortly joined the Massachusetts Medical Society. In actual practice he seems to have had only moderate success. It is doubtful if he ever cared much for the life of a general practitioner. And he admitted that he did not make any strenuous efforts to build up a practice. Probably he did not add many to his list of patients by publishing a book of youthful poems just a year after his return from Europe. He competed successfully for the Boylston Prize in 1836 and 1837, winning three out of the four prizes offered by writing dissertations on "Indigenous Intermittent Fever in New England," "Neuralgia," and "The Utility and Importance of Direct Oral Examination in Medical Practice." The first of these is still a medical classic. In it Dr. Holmes displayed his accurate historical sense and has gathered together all that is known of malaria, its distribution, symptoms, etc., in the early settlement of New England.

In 1838 he was appointed Professor of Anatomy and Physiology in Dartmouth College at Hanover, but resigned after a year or two. He was married in 1840 to Miss Amelia Lee Jackson, a niece of his old preceptor. Dr. Holmes, in addition to his writings, together with three friends, engaged in teaching at the Tremont Street Medical College, a kind of supplementary institution to the Harvard Medical School, and in association with Dr. Bigelow he edited the American edition of Marshall Hall's text-book on the Theory and Practice of Medicine.

In 1842 he published two lectures on "Homeopathy and its Kindred Delusions." In them various senseless medical fads are playfully reviewed. The reader is introduced to the Royal cure of the King's Evil, the Weapon Ointment, which was applied to the weapon producing the wound for its healing, the Tar Water Mania of Bishop Berkely, and the "metallic tractors" of Mr. Perkins. Homeopathy, which he had doubtless become familiar with in Paris, is discussed in no stinted language in the second lecture. The good doctor hated homeopathy with a whole-souled hatred. He spoke of it as a "pseudo science." He showed its inconsistencies and absurdities. The argument founded on its occasional good results would be just as applicable, he said, to the counterfitter who gives base coin on the ground that a spurious dollar had often relieved a poor man's necessities.

The parallel which the homeopathists attempted to draw between the effects of their infinitesimal doses and the production of small-pox from minute quantities of animal vaccine he shatters with the suggestion that the mind advancing this argument could reason that "a pebble may produce a mountain because an acorn can become a forest, or that because a

spark will burn down a city a mutton-chop will feed an army."

He refers to the absurdity of the original contention of Hahnemann, the founder of the cult, that seven-eighths of all chronic diseases are the result of psora, a skin affection called the itch.

He points out that to show the axiom "Similia Similibus Curantur" (like is cured by like) to be the sole law of nature in therapeutics, it is necessary to establish that drugs are always capable of curing diseases most like their own symptoms and that remedies should be shown not to cure diseases when they do not produce symptoms resembling those presented in these diseases. Neither of these propositions has ever been established. He predicts that the "Semi-Homeopathist will gradually withdraw from the 'rotten half of his business and try to make the public forget his connection with it and the ultra-Homeopathists will either recant or embrace some new and equally extravagant doctrine'; very few will stick to their colors and go down with their sinking ship."

Unquestionably Dr. Holmes' most important contribution to medicine was made in 1843, when he read before the Boston Society for Medical Improvement an essay on the Contagiousness of Puerperal Fever. This was published in the New England Quarterly Journal of Medicine and Surgery for April of that year. The journal soon ceased to be published and the essay can hardly be said to have been brought before the profession.

It must be recalled that this was long before the days when the nature of contagion was understood and several years before the extended researches of Semmelweis[2] on the same subject. Holmes, in his original essay, which he republished unchanged twelve years later, marshals a startling number of cases of puerperal fever presumably carried to the mother by the attending physician or nurse. He points out clearly the probable connection between erysipelas and child-bed fever. His contention met with violent, almost contemptuous opposition from the leading obstetricians of the day, notably by Drs. Hodge and Meigs, of Philadelphia. The latter wrote in 1852: "I prefer to attribute these cases to accident or Providence, of which I can form a conception, than to a contagion of which I cannot form any clear idea"; and Hodge advises his students to "divest their minds of the overpowering dread that you can ever become the minister of evil, that you can ever convey in any possible manner a horrible virus so destructive in its effects and so mysterious in its operations as that attributed to puerperal fever."

In republishing the essay in 1855, Holmes makes an earnest plea to students for freedom from the trammels of authority, for individual judgment of facts. "Students," he says, "have naturally faith in their instructors, turning to them for truth and taking what they may choose to give them: babes in knowledge, not yet able to tell the breast from the bottle, pumping away for the milk of truth at all that offers were it nothing better than a professor's shrivelled forefinger."

The rules for the guidance of physicians in midwifery practice laid down by Holmes in 1843 need little revision to-day:

"1. A physician holding himself in readiness to attend cases of midwifery should never take any active part in the post-mortem examination of cases of puerperal fever.

"2. If a physician is present at such autopsies, he should use thorough ablution, change every article of dress, and allow twenty-four hours or more to elapse before attending to any case of midwifery. It may be well to extend the same caution to cases of simple peritonitis.

"3. Similar precautions should be taken after the autopsy or surgical treatment of cases of erysipelas, if the physician is obliged to unite such offices with his obstetrical duties, which is in the highest degree inexpedient.

"4. On the occurrence of a single case of puerperal fever in his practice, the physician is bound to consider the next female he attends in labor, unless some weeks at least have elapsed, as in danger of being infected by him, and it is his duty to take every precaution to diminish her risk of disease and death.

"5. If within a short period two cases of puerperal fever happen close to each other, in the practice of the same physician, the disease not existing or prevailing in the neighborhood, he would do wisely to relinquish his obstetrical practice for at least one month, and endeavor to free himself by every available means from any noxious influence he may carry about with him.

"6. The occurrence of three or more closely connected cases, in the practice of one individual, no others existing in the neighborhood, and no other sufficient cause being alleged for the coincidence, is prima facie evidence that he is the vehicle of contagion.

"7. It is the duty of the physician to take every precaution that the disease shall not be introduced by nurses or other assistants, by making proper inquiries concerning them, and giving timely warning of every suspected source of danger.

"8. Whatever indulgence may be granted to those who have heretofore been the ignorant causes of so much misery, the time has come when the existence of a private pestilence in the sphere of a single physician should be looked upon, not as a misfortune, but a crime; and in the knowledge of such occurrences the duties of the practitioner to his profession should give way to his paramount obligations to society."

The earnestness of the writer, to whom hundreds of mothers owe their lives, is attested by the closing paragraphs of the original paper:

"The woman about to become a mother, or with her newborn infant upon her bosom, should be the object of trembling care and sympathy wherever she bears her tender burden, or stretches her aching limbs. The very outcast of the streets

[2] J. P. S. Semmelweis was born in 1818, and graduated in Medicine in 1846. Shortly after this time he became interested in the study of Child-bed fever. He probably considered it contagious as early as 1849, and defended his contentions in numerous personal letters, written between 1858 and 1860. His first formal publication on the subject, entitled: "Die Aetiologie der Begriff und die Prophylaxis des Kindbettfiebers," appeared in 1861.

has pity upon her sister in degradation, when the seal of promised maternity is impressed upon her. The remorseless vengeance of the law, brought down upon its victim by a machinery as sure as destiny, is arrested in its fall at a word which reveals her transient claim for mercy. The solemn prayer of the liturgy singles out her sorrows from the multiplied trials of life, to plead for her in the hour of peril. God forbid that any member of the profession to which she trusts her life, doubly precious at that eventful period, should hazard it negligently, unadvisedly, or selfishly!"

In the "Professor at the Breakfast Table," he said, "I held up to the professional public the damnable facts connected with the conveyance of poison from one young mother's chamber to another's, for doing which humble office I desire to be thankful that I ever lived, though nothing else good should ever come into my life."

Holmes' graceful pen was soon recognized and he was asked to lecture, much to his personal inconvenience, in the many towns about Boston. He kept up his interest in medical history and practice, however, and gave some instruction in the use of the microscope, which instrument he was among the first to use in this country. He had unusual mechanical skill and was interested in the adjustment of the lens almost as much as in the study of the specimen, although he did describe some cells at the ends of long bones in a paper which he read at a medical gathering in 1851. Later he invented a stereoscope for hand use, described as an exceedingly clever device, which if patented might have made him for those times a rich man.

In 1847, at the age of 38, Holmes was elected Professor of Anatomy and Physiology at Harvard Medical School, which position he held continuously for thirty-five years, although the Chair of Physiology was separated in 1871.

As a lecturer in anatomy Holmes became immediately popular. He knew his subject well and loved it, and was able to enliven his lectures with witty allusions which fixed the object in the students' memory. "Gentlemen," he said on one occasion, holding up a female pelvis, "this is the triumphal arch under which every candidate for immortality has to pass." Again, "These, gentlemen," pointing to the lower portion of the pelvic bones, "are the tuberosities of the ischia, on which man was designed to sit and survey the works of Creation."

His lecture-room was in an old building and to reach it Holmes had to climb up a pair of dark, winding stairs, often, because of his asthma, with the help of the janitor.

He lectured five times a week during the session at one o'clock, after the students had had previously four weary hours of continuous talk. Holmes was the only one who could interest them during the last hour.

Dr. Chever, one of his demonstrators, thus vividly describes the scene, so familiar to his students, but strange to those who only knew Holmes as the writer of graceful English:

"It nears one o'clock, and the close work in the demonstrator's room in the old Medical School in North Grove Street becomes even more hurried and eager as the lecture hour in anatomy approaches. Four hours of busy dissection have unveiled a portion of the human frame, insensate and stark, on the demonstrating-table. Muscles, nerves, and blood-vessels unfold themselves in unvarying harmony, if seeming disorder, and the 'subject' is nearly ready to illustrate the lecture. . . . The room is thick with tobacco smoke. The winter light, snowy and dull, enters through one tall window, bare of curtain, and falls upon a lead floor. The surroundings are singularly barren of ornament or beauty, and there is naught to inspire the intellect or the imagination, except the marvellous mechanism of the poor dead body, which lies dissected before us, like some complex and delicate machinery whose uses we seek to know.

"To such a scene enters the poet, the writer, the wit, Oliver Wendell Holmes, and asks, 'What have you for me to-day?' and plunges, knife in hand, into the 'depths of his subject,'—a joke he might have uttered. Time flies, and a boisterous crowd of turbulent Bob Sawyers pours through the hall to his lecture-room, and begins a rhythmical stamping, one, two, three, and a shout, and pounding on his lecture-room doors. A rush takes place; some collapse, some are thrown headlong, and three hundred raw students precipitate themselves into a bare and comfortless amphitheatre. Meanwhile the professor has been running about, now as nimble as a cat, selecting plates, rummaging the dusty museum for specimens, arranging microscopes, and displaying bones. The subject is carried in on a board; no automatic appliances, no wheels with pneumatic tires, no elevators, no dumb-waiters in those days. The cadaver is decorously disposed on a revolving table in the small arena, and is always covered, at first, from curious eyes, by a clean, white sheet. Respect for poor humanity and admiration for God's divinest work is the first lesson and the uppermost in the poet-lecturer's mind. He enters, and is greeted with a mighty shout and stamp of applause. Then silence, and there begins a charming hour of description, analysis, simile, anecdote, harmless pun, which clothes the dry bones with poetic imagery, enlivens a hard and fatiguing day with humor, and brightens to the tired listener the details of a difficult though interesting study. We say tired listener because—will it be believed?—the student is now listening to his fifth consecutive lecture that day, beginning at nine o'clock and ending at two; no pause, no rest, no recovery for the dazed senses, which have tried to absorb Materia Medica, Chemistry, Practice, Obstetrics, and Anatomy, all in one morning, by five learned professors. One o'clock was always assigned to Dr. Holmes because he alone could hold his exhausted audience's attention.

"As a lecturer he was accurate, punctual, precise, unvarying in patience over detail, and though not an original anatomist in the sense of a discoverer, yet a most exact descriptive lecturer; while the wealth of illustration, comparison, and simile he used was unequalled. Hence his charm; you received information, and you were amused at the same time. He was always simple and rudimentary in his instruction. His flights of fancy never shot over his hearers' heads. 'Iteration and reiteration' was his favorite motto in teaching.

"And how he loved Anatomy! as a mother her child. He

was never tired, always fresh, always eager in learning and teaching it. In earnest himself, enthusiastic, and of a happy temperament, he shed the glow of his ardent spirit over his followers, and gave to me, his demonstrator and assistant for eight years, some of the most attractive and happy hours of my life."

Holmes took the liveliest interest in the Medical School. He was Dean from 1847 to 1853. He was always accessible to the students and ready to give them kindly counsel.

He never was a strict disciplinarian and confessed that when he examined a man who was to live on 25-cent fees he usually confined his questions to the biceps.

President Eliot said of Holmes at a Congratulatory Breakfast: "He was one of the most active and hard-working of our lecturers. I never knew any other mortal exhibit such enthusiasm over an elegant dissection. Perhaps you think it is with the pen that Dr. Holmes is chiefly skillful. I assure you he is equally skillful with the scalpel and microscope. He knows every bone, muscle, artery, and nerve, and describes them with fascinating precision. Traces of his life work occur on every page of his writings."

During Holmes' connection with the school there was a violent discussion in the faculty as to the advisability of admitting women students. He took no decided stand at the time, but later in an address made certain remarks which were probably his views on this interesting topic.

A short time afterward, when the smoke of this battle was lifting, if not quite all gone, at the opening of the new building of the Harvard Medical School, Dr. Holmes delivered an address, and Professor Dwight told the following anecdote:

"On this occasion, after speaking in his most perfect style on woman as a nurse, with a pathos free from mawkishness which Dickens rarely reached, he [Holmes] concluded: 'I have always felt that this was rather the vocation of woman than general medical, and especially surgical, practice.' This was the signal for loud applause from the conservative side. When he could resume he went on: 'Yet I myself followed the course of lectures given by the young Madame Lachapelle in Paris, and if here and there an intrepid woman insists on taking by storm the fortress of medical education, I would have the gate flung open to her, as if it were that of the citadel of Orleans and she were Joan of Arc returning from the field of victory.' The enthusiasm which this sentiment called forth was so overwhelming, that those of us who had led the first applause felt, perhaps looked, rather foolish. I have since suspected that Dr. Holmes, who always knew his audience, had kept back the real climax to lure us to our destruction."

He said he was willing to teach women anatomy but not in the same classes or dissecting-rooms with men.

Few members of the profession have been so well versed in medical literature as was Dr. Holmes. He knew the worthies and their writings from Hippocrates down. He said on presenting his loved collection of one thousand volumes and many pamphlets to the Boston Medical Library, an institution largely due to his name and influence, and of which he was president for thirteen years: "These books were very dear to me as they stood on my shelves. A twig from some one of my nerves ran to every one of them." A visitor at his home describes his joy when a copy of the original edition of Vesalius came from New York. He was fond of showing to agents for new anatomical books how superior were the illustrations in the works of some of the old writers.

When James Russell Lowell became editor of the Atlantic Monthly in 1857 he persuaded Dr. Holmes to contribute. This resulted in the Autocrat of the Breakfast Table, which immediately placed the author in the first rank of writers of sprightly English.

His literary prominence and the establishment at about the same time of the famous Saturday Club, which included among its members Emerson, Hawthorne, Whittier, Longfellow, Lowell, and Motley, gradually absorbed more and more of Holmes' interest and time.

The demands upon his muse were incessant, but were for the most part complied with. Literature, however, never really weaned him from the science of medicine, although it put a conclusive end to his practice as a physician.

As the years went by Dr. Holmes was called upon to make many addresses on occasions before medical meetings and various classes of medical students. These addresses for the most part have been gathered together in his volume of Medical Essays. They show the richness of his scholarship and his familiarity with a great variety of scientific topics and with all his kindliness and common sense.

He was a strong believer in expectant treatment, or at least in moderate and definite therapeutics, and in the self-limitation of disease as championed by Dr. James Jackson. "The traditional idea," he declares, "of always poisoning out disease as we smoke out vermin is now seeking its last refuge."

"Young man," he asks, "are you sure you cured your patient? if so, perhaps to-morrow you may kill—but then you say the patient died."

"From the time of Hippocrates," he adds, "to that of our own medical patriarch there has been an apostolic succession of wise and good practitioners who place before all remedies the proper conduct of the patient."

The assertion in a lecture on Scholastic and Bedside Teaching delivered in 1867, that the most essential part of a student's instruction is obtained not in the lecture-room but at the bedside, sounds strangely familiar, and comes with good grace from a lifelong lecturer.

His address on "the young practitioner," delivered to the class leaving Bellevue in 1871, deserves to be repeated each year to the graduate of all our medical colleges.

The influence of his professional training was exerted not only in these dissertations but permeated every page he penned. He wrote, he asserted, "medicated novels" and medical terms are frequent in his writings.

"A laugh at an entertainment," he says, "broke out prematurely. It was a sporadic laugh and did not become epidemic."

His interest in psychological problems in the power of

heredity and its effect on moral responsibility, appear in many of his works.

The scriptural limit of three score years and ten Dr. Holmes vivifies in these familiar words:

"Our brains are seventy year clocks. The Angel of Life winds them up once for all, then closes the case and gives the key to the Angel of Resurrection. Tic tac! tic tac! go the wheels of thought; our will cannot stop them; they cannot stop themselves; sleep cannot still them; madness only makes them go faster; death alone can break into the case, and, seizing the ever-swinging pendulum, which we call the heart, silence at last the clicking of the terrible escapement we have carried so long beneath our wrinkled foreheads."

Oliver Wendell Holmes stood as a constant protest against the depicting of gross and suggestive quasi-medical scenes in literature. He said that when "Zola and his tribe crossed the borders of science into its infested regions, leaving behind them the reserve and delicacy which the genuine scientific observer never forgets, they disgust even those to whom the worst scenes are too wretchedly familiar."

On retiring from his active teaching in 1882, his thought was not to rest but to devote his time more continuously to writing. He said in a letter that he "had taken off his professor's gown and was in his literary shirt sleeves." Apparently he never again gained the heights reached in the heyday of his genius, but he still wrote acceptably and with much of his old brightness to a large company of appreciative readers.

In 1886, in company with his daughter, Holmes made a hurried trip to Europe, the first since his student days more than a half-century before. His journey through England was a triumphal procession. He received honorary degrees at Oxford, Cambridge, and Edinburgh, and was the recipient of the kindliest hospitality wherever he went, as his name had been for years a household one in England. While there, two important medical treatises were dedicated to his honor. He crossed to Paris for a week spent in visiting his old haunts and marked the many changes the political vicissitudes had brought about in that city. He called upon Pasteur in his laboratory, and speaks with the utmost appreciation of the latter's scientific labors and his great benefactions to mankind.

A year or two after his return he lost his wife, who had been his devoted companion for nearly fifty years; who had shielded him in every possible way and made his home his chief delight amid all his unusual pleasures.

His widowed daughter, Mrs. Sargent, who had come to care for him, died the year after her mother, and in 1889 he made his home in the family of his distinguished son, Mr. Justice Holmes.

Dr. Holmes felt keenly the passing away of his friends and contemporaries. He writes to one of his few remaining cronies: "The Keystone of our Arch has fallen; all we can do is to lean against each other until the last stone is left standing alone."

He did indeed live to be nearly "the last leaf upon the tree, in the spring." His physical powers were maintained with almost undiminished vigor to the end. He spent the summers at his cottage at Beverly Farm on the coast. Here he received in the most delightful kindliness many visitors who called to do reverence to the genial doctor, the sprightly autocrat, and the best talker in America. They never were disappointed. During a morning spent with the editor of the British Medical Journal who was in this country and made the usual pilgrimage to Beverly Farm, Dr. Holmes, after inquiring after many of his medical friends in England, remarked that he had passed the best years of his life as a doctor, "and I hope," he said, "they are not ashamed of me and do not reproach me for choosing to tread the flowery path of very light literature rather than chain myself for ever to the heavy tasks of medical practice." He needed to have no fears, for he, like William McClure in a very different sphere, was an honor to the profession.

> And if for some I keep a nobler place;
> I keep for none a happier than for thee.
>
> —*Macaulay.*

THE BLOOD IN PERNICIOUS ANÆMIA.

By CHARLES PHILLIPS EMERSON, M. D.,

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In this study of eighty-nine cases of pernicious anæmia a few features of this disease are considered from the viewpoint of the blood. We do not present any new discoveries concerning the disease, merely a few details in an as yet incomplete clinical picture.

The rule of this clinic is that at least one complete blood examination shall be made weekly in all cases of pernicious anæmia but these examinations are usually made twice weekly. We have tried to avoid deductions made from few counts, and when we speak of a "period with rising" or "falling count" we believe that we have records of sufficient blood examinations to be sure that such was the course of the blood during that period.

Several of these eighty-nine cases here mentioned were admitted more than once, hence the total number of admissions is one hundred and eight.

Primary pernicious anæmia is a disease the real causes of which are yet to be discovered, and at autopsy no lesion sufficient to explain the anæmia is to be found; hence the term "primary" anæmia. Clinically it is a very severe anæmia with signs both of blood destruction and of abnormal, or at least imperfect, regeneration. The signs of blood destruc-

tion are: the low count, the degenerations seen in the red cells, the slight jaundice, the increased urinary pigments, the occasional hæmoglobinæmia, and the increase of iron stored in the liver, spleen, and other internal organs. The evidences of abnormal regeneration are: the cells of abnormal size (macrocytes and microcytes), the distorted cells (poikilocytes), and the unusual forms of nucleated reds (megaloblasts, intermediates). There is oligochromæmia of a marked degree; the hæmoglobin runs almost parallel to the count of red cells, but the color index is usually above 1. The leucocytes are usually diminished in number, but the small mononuclear cells are always relatively, and sometimes absolutely increased. The platelets are diminished.

When studying cases of pernicious anæmia one is impressed by two features: the nonparallelism between the blood picture and the subjective symptoms, and the constant ebb and flow of the red-cell count. One sees men able to lead active business lives with only 1,000,000 red cells per cubic millimeter. Indeed, the low counts on first admissions show how severe an anæmia must be before the patients give up and consult a physician. Cases of chlorosis suffer much more when the count is about 4,000,000 cells per cubic millimeter. Again, the count seldom remains stationary, but is either rising or falling. The contrast is well seen in cases of the anæmia of myxœdema or cancer, where constancy is the rule. For the count in a given case to remain constant for any length of time is evidence against the diagnosis of pernicious anæmia. It is either rising or falling, the rate of increase and decrease sometimes being quite uniform; the periods of improvement and of relapse often succeed each other with a singular rhythm, frequently independent of subjective sensations, and almost of medication.

The Red Corpuscles.—*Count on Admission.*—The count on admission will depend on the symptom or symptoms for which the patient seeks relief. In general it is true that the first counts on these patients are the lowest of any group. To find the red-cell count under 1,500,000 in a patient who has no very evident cause for anæmia, who has not been under treatment, is almost sufficient for diagnosis.

Of our 108 first counts (of 89 patients—some had several admissions), the

lowest was 516,000			
below 1,000,000, 17, or 16% of the admissions,			
between 1,000,000	and	2,000,000, 56, or 52%,	
" 2,000,000	"	3,000,000, 16,	" 15%,
" 3,000,000	"	4,000,000, 17,	" 16%,
above 4,000,000		2,	" 1%,

Our cases may roughly be divided into three groups, according to the symptoms of which the patients complain: First, there are those who mention only the "shortness of breath and weakness on exertion," which seem due to the profound anæmia. These patients come in with the lowest counts. Second, there are those with gastro-intestinal symptoms; nausea, vomiting, diarrhœa, constipation, dyspepsia, etc. These symptoms begin earlier, hence these patients are admitted with counts between 1,000,000 and 2,000,000. The patients of the last group come for a varied list of ailments, but common among them are those due to a combined sclerosis which is sometimes a very early feature. Case 80 on his second admission complained of numbness in the legs, and had a count of 4,276,000, the highest first count of our series. Upon symptoms also will depend the time the patient can be persuaded to stay in the hospital, and hence the *count on discharge*. It is hard for him to accept our idea of the severity of his condition, and if he does not, he leaves when the symptoms which brought him to the clinic have disappeared. Patients of the first group who have really suffered from the weakness of the anæmia are usually willing to stay a reasonable length of time. Patients of the third group, especially those with nervous features, stay the longest; but patients of the second group, who come with gastro-intestinal symptoms, stay a short time only, since these symptoms are soon corrected, and the weakness dependent on them disappears.

Course, as judged by the red cells.—In a few rare cases the count remains quite stationary while the patient subjectively improves and soon feels so well that he insists on his discharge. Of these we cite 7 cases:

Case 70 was admitted complaining of poor digestion and general weakness, and with a red count of 1,600,000. The cells varied little and in 20 days he was discharged with 1,400,000 cells and feeling much improved. He rested a few days at home and then returned to work.

Case 69 on admission had 1,500,000 red cells. He complained of dysentery and weakness. The counts varied from 1,842,000 to 1,328,000. In 74 days he was discharged feeling much better, the count being 1,836,000.

Case 68 came in for diarrhœa and weakness with a count of 1,040,000 red cells. During 63 days the maximum count was 1,979,000 and the lowest that on admission. At the end of that time he left with a count of 1,448,000 red cells, feeling better.

Case 55 complained of indigestion, loss of weight and strength; the count was 1,368,000. During 46 days the highest count was 2,100,000, the lowest 1,368,000, and on discharge, 1,800,000. He left much improved.

Case 45 was admitted with 1,760,000 red cells and complained of "stomach trouble, pain in the liver, and weakness." During 17 days the highest count was 2,246,000, the lowest 1,700,000. He was then discharged in good condition, with a count of 1,724,000.

Case 83.—On admission the count was 1,604,000. During 109 days the red cells varied from 1,988,000 to 1,482,000, and at the end the count was 1,552,000.

Case 88.—On admission the count was 804,000. He was in the hospital 9 days. The maximum count was 1,092,000, the minimum, 804,000; at the end the count was 940,000.

These cases are interesting since they all belonged to the group mentioned above of patients who come for gastro-intestinal symptoms. They felt well enough to go home and some to work, when the count was much the same as that on admission.

Another group consisted of 24 cases whose counts rose steadily from admission till discharge. Of these, 13 left with counts between 3,000,000 and 4,000,000 and 3 with higher This represents a gain of from 40 to 260 per cent, with an average of 140 per cent, and this gain required from 30 to 120 days under treatment.

A group of 46 cases remained until the red cells had practically ceased to rise, although during the stay the counts had fluctuated considerably. In 22 of these cases the final count was between 2,800,000 and 3,800,000 red cells per cubic millimeter.

It is very difficult to get the cells to rise above 4,000,000 per cubic millimeter, and if after the cells have reached that point the patient remains in the hospital one may have the disappointment of seeing the fall of the wave. The count usually remains about 4,000,000 during the intermissions, a point of great importance in the diagnosis of the case during those periods. Two cases have recently been brought to our notice who, during intermissions, had taken as heavy life insurance as they could. Their brown pigmented, "sunburned" skin, their rather pale lips, and tinted scleræ did not attract attention. Both died within a year after their insurance examinations.

The count seldom remains constant, it usually rises or falls in regular, periodic waves. An illustration of this *periodicity* is Case 83. The cells rose for 17 days, 19,000 cells a day. They then fell for 30 days, 15,000 a day. They next rose 16,600 per day for 30 days, and then fell 13,000 per day for 32 days. The regularity of the periods and the constancy of rate of rise and fall is interesting.

Changes in the red count may be due to new formation or destruction of red cells, or to changes in the volume of the plasma. We believe the rises so often seen before death and which simulate improvement are of this latter nature.

The rate of rise and fall is interesting. During 37 periods of genuine improvement the cells rose from 30,000 to 50,000 cells per day in 16 cases, less than 30,000, in 13 cases, and over 50,000 cells per day in 8 cases. The highest was 107,000 per day. Those cases who were really "getting well" gained from 50,000 to 70,000 cells per day; we refer to the cases whose progress was clinically rapid and very satisfactory. Of 13 cases in which the rising count did not seem to mean improvement in 8 the gain was from 10,000 to 30,000, and in 4 from 30,000 to 50,000 cells per day. Of the 37 cases with genuine improvement in 10 there was a blood crisis during these periods. The gain in 6 of these 10 was from 30,000 to 66,000 cells a day. The cases with eosinophilia gained from 1000 to 80,000 cells a day. The time over which these rises extended lasted roughly from 4 to 6 weeks. Of the 16 cases mentioned above with gains of from 30,000 to 50,000 cells a day, in 14 it lasted from 4 to 9 weeks, and in one, 12 weeks. The gain of 66,000 cells a day lasted 6 weeks. Of the 13 cases with unprofitable rises, in 5 it lasted 2 weeks, and in 8 from 3 to 7 weeks.

The rate of fall was somewhat slower. Of 39 cases with periods of falling counts, in 10 the loss was from 20,000 to 30,000 cells a day, and in 25 from 10,000 to 40,000. The falls of from 20,000 to 30,000 cells per day lasted longest, from 9 to 130 days, an average of 37 days. The losses of from 1000 to 10,000 lasted on an average for 35 days. The worst loss was of 233,000 cells a day for 3 days.

Among our cases which were interesting as regards *the counts on admission and discharge,* the following groups may be cited: In one group the subjective improvement occurred during a falling count. The number of cells first rose, then fell, and the patient left when the count was about that on admission. Case 35 was admitted for "sore mouth, heartburn, and numbness and tingling of both hands." The red count was 1,908,000 per cubic millimeter. It rose for 14 days to 2,996,000 and then fell to 2,120,000, on which date he went home "well." It is interesting to note how little relation his count bore to his feelings.

More cases were admitted with a falling count, which was soon succeeded by a rising one. With the rise there was improvement in symptoms and the patient insisted on leaving when the count was practically that on admission. In Case 38 the count on admission was 2,930,000. It fell for 3 days to 2,236,000 and then rose for 8 days to 3,004,000, when he was discharged. In Case 75 the count on admission was 1,760,000. It fell for 38 days to 792,000, and then rose for 45 days to 1,624,000, at which time he was discharged. In Case 81 the count on admission was 1,756,000. It fell for 23 days to 1,373,000, and rose during the next 35 days to 1,762,000. He then was discharged.

In another group of cases the count first rose for a variable time, and the patients seemed to improve. Then it fell until death. The final count at death was sometimes almost the same as that on admission. Case 27 had on admission 767,000 cells per cubic millimeter. In 3 days it had risen to 940,000, but then began to fall, reaching in 24 days, 557,000 cells on the day of death. Case 46 had on admission 940,000 cells. At the end of 24 days the count was 1,023,000. Six days later at death it was 718,000. Case 65 is a very good illustration. This patient was admitted for "sick stomach, sick bowels, shortness of breath," and a count of 1,236,000. At the end of 63 days the count was 3,428,000. In 224 days it had fallen to 840,000, and in 18 days had risen to 1,216,000. He died the day following, and at autopsy only the lesions of a severe anæmia were found.

In some cases the count rises from the day of admission till that of death. To explain this, changes in the volume of plasma may be important. Case 78 on admission had 1,228,000 red cells. At the end of 19 days the count was 1,864,000, 8 days later it was 2,144,000, and death followed.

Another group of cases similar to this has first a falling count which then rises and continues to rise until death. Case 76 had on admission 1,192,000 cells. In 28 days it had fallen to 828,000. It then rose and in 12 days was 1,028,000. Four days later the patient died.

A recent case not included in the above series shows this

even better. The course of this patient was clinically downward during the whole period in the ward.

Date.	Reds.	Leucocytes.
July 18.....	1,550,000	4,700
" 25.....	1,815,000	7,300
Aug. 4.....	1,560,000	3,600
" 13.....	1,839,000	2,400
" 21.....	1,692,000	6,800
" 28.....	1,496,000	2,200
Sept. 11.....	1,490,000	4,000
" 25.....	1,690,000	4,800
Oct. 5.....	1,962,000	3,300
" 12.....	2,132,000	4,320
" 21.....	2,632,000	3,280
" 30.....	2,000,000	1,860
Nov. 7.....	2,860,000	1,560

The count at death is of even greater interest than that on admission. The following are all counts made within 48 hours of death:

376,000	..... the lowest,	
400,000 to 500,000	..... 3 cases,	
500,000 to 600,000	..... 3 cases,	
600,000 to 700,000	..... 4 cases,	
864,000	..... 1 case.	
	Mean of above 12 cases.....	540,000.
1,000,000 to 1,100,000	..... 4 cases,	
1,100,000 to 1,200,000	..... 1 case,	
1,200,000 to 1,300,000	..... 1 case,	
1,300,000 to 1,400,000	..... 2 cases.	
	Mean of above 8 cases.....	1,100,000.
2,144,000	..... 1 case,	
2,704,000	..... 1 case.	

One is tempted to divide these cases, according to the counts at death, into three sharply-defined groups, for it seems improbable that the above arrangement could be accidental. But further consideration shows that the cases are here grouped much as they were on admission. Of the first 12 cases the highest on admission was 2,048,000, the mean of all being 1,064,000, and the average of all 1,100,000; 5 were below 1,000,000. Of the 8 cases of the second group the average on admission was 1,442,000, the lowest being 1,192,000 and the highest 1,992,000. Of the 2 cases with highest counts the first counts were 1,800,000 and 2,240,000. It would seem from these few cases that the higher the count with the first symptoms, the higher it is at death.

The immediate causes of death in this disease are many. Some patients show progressive weakness and dyspnœa, are irrational, and seem to die from weakness alone. Some of these at autopsy have œdema of the lungs, but no lesions to explain death other than those of a severe anæmia. Others die of terminal infections. Eight of the 12 cases of the first group had clinically and at autopsy no cause of death, save the signs of anæmia. One died suddenly and 2 of terminal infections. Four of the second group died of terminal infections and two of "anæmia." Both of the cases of the third group died of "anæmia."

Counts on successive admissions.—While different persons come with widely different counts it often happens that the same person will come at different times with counts curiously similar, as if each person had a limit below which the red cells could not fall without symptoms severe enough to induce him to seek relief. Of course this is not always the case.

Twelve of our cases were admitted more than once; in 10 the count on second admission was lower than that on the first.

Case 68.—First count on admission was 1,060,000; on the second, 26 days later, 1,040,000.

Case 76.—On first admission the first count was 1,206,000, the last was 4,080,000. Four months later he was readmitted with a count of 1,192,000.

Case 67.—On the first admission the first count was 1,300,000, the last was 3,890,000. He was readmitted in four months' time with a count of 1,090,000.

Case 82.—On the first admission the first count was 1,928,000, the last was 2,448,000. After 13 months he returned with a count of 1,620,000, and was discharged later with the count about the same. Fourteen months later he returned with a count of 1,864,000, and was discharged with a count of 2,900,000. The fourth admission was 11 months later, and the first count was 1,638,000. At death it was 376,000.

All of the cases admitted more than once had moderately high counts at first. None were admitted with low counts.

Just as some persons are "well" when the count is about that of admission, so some die with a count which has hardly changed.

Case 9 on admission had 672,000 red cells. In ten days there was no change, and the last count was 648,000. He died two days later.

Case 19 was admitted with 516,000 cells and died four days later with 454,000.

Thirteen of our 22 fatal cases answered the description of the older writers who defined pernicious anæmia as one which progresses on a downward course relentlessly to death. A good illustration of this is the following:

Case 82 (fourth admission). We give only a few of the 42 blood examinations made.

Date.	Reds.	Hb.	Leuco.	Remarks.
Jan. 9, '04....	1,638,000	40	3000	Mononuclears 42%.
" 14, ...	1,427,000	35	3100	
" 21, ...	1,654,000	43	4100	
" 28, ...	1,515,000	35	4700	
Feb. 1, ...	1,332,000	35	3000	
" 5, ...	1,260,000	30	3600	An ineffectual blood crisis begins.
" 9, ...	1,092,000		2800	Normoblasts 896, Intermediates 4368, Megaloblasts 784 per cubic millimeter.
" 13, ...	1,064,000	27	3200	
" 16, ...	1,280,000	32	2700	Crisis at end.
" 21, ...	1,000,000	25	3500	
" 24, ...	1,064,000	27	2500	
" 27, ...	860,000	27	3200	
Mar. 2, ...	700,000	25	3400	A few nucleated reds.
" 6, ...	764,000	23	1200	Mononuclears 62%.
" 9, ...	648,000	20	1500	No nucleated reds.
" 13, ...	570,000	17	2400	
" 15, ...	376,000	13	3300	Death.

Nucleated Red Cells.—A discussion of this question

should not be begun before definitions are given of the terms to be used. One reason there is such confusion concerning the occurrence of these cells is that one man calls a megaloblast a cell which others would class as an intermediate or even a normoblast. Normoblasts are, we believe, nucleated red cells, the size of the ordinary non-nucleated cells, perhaps a trifle larger, with a nucleus about 3.5 microns in diameter, round, and sharply defined. The larger nuclei have a perfect chromatin network; these cells are called "Howell's immature nucleated reds"; other cells having smaller nuclei which are very dense, stain deeply and diffusely, and which show absolutely no trace of a chromatin network, "Howell's mature cells." Between the two extremes are cells with nuclei showing every step in the process of pycnosis. All these we group as normoblasts, although many call the immature cells intermediates. By megaloblast we mean a large nucleated red with nucleus at least 7 microns in one diameter; that is, about the size of an ordinary red cell. The protoplasm may be polychromatophilic, with ragged edge, the nucleus oval, staining faintly, with a fine chromatin network of definite pattern, separated from the protoplasm by a colorless line, and with other characteristics sometimes urged as necessary to its identification but the one essential thing, we believe, is a nucleus the size of an ordinary red blood cell. Our reason for this as the criterion is the result of the study of many bone-marrows of ribs of infants, removed at operation, and at early autopsies. In all were found two types of cells with constant characteristics; the normoblasts, and cells with nuclei over 7 microns in diameter. In addition to these are cells without constant points in size, with nuclei varying from those of immature reds to those of megaloblasts. These were called intermediate nucleated reds, and may be defined as cells with bodies too large for normoblasts or nuclei too small for megaloblasts. They may perhaps have about the same significance as melagoblasts, but our rule is to call every cell concerning which there is any doubt, an intermediate. We do not count the immature cells in this group. It would seem that red cells are produced in "islands of proliferation" with megaloblasts at the center and normoblasts on the periphery, and that in perniciaus anæmia these islands are stripped of their outer zones leaving the megaloblasts to keep up the supply of red cells (Bunting).

Nucleated reds were present at some time in 62 of 74 cases; normoblasts alone in 11; normoblasts, intermediates, and megaloblasts in 45; megaloblasts and intermediates in 6. In 61 cases there were 67 periods during which nucleated cells were present for a considerable time. During 27 (44 per cent) of these periods the red cells rose; during 34 (56 per cent) they remained stationary or fell. Fourteen other periods of about equal length were chosen during which no nucleated cells at all were found, and during 8 of these red cells rose.

Hæmoglobin.—The hæmoglobin is reduced to a low point, yet apparently not to quite so low a one as the count of the red cells. In our cases it was on admission, from

10 to 20%	in 19	cases,	a.
20 " 30%	" 26	"	b.
30 " 40%	" 32	"	c.
40 " 50%	" 19	"	d.
50 " 60%	" 4	"	e.
60 " 70%	" 2	"	f.
70 " 80%	" 1	"	g.

Since the reduction of hæmoglobin is not quite as great as that of red cells, the *color index* (hæmoglobin per cent divided by red cell per cent, 5,000,000 = 100 per cent) is usually greater than 1.

Index.	a	b	c	d	e	
0.6 to 1.0.....	3	9	5	1	1	total 19
1.0.....	6	4	10	5	0	" 25
1.0 " 1.5.....	6	11	15	11	3	" 46
1.5 " 1.9.....	4	2	2	2	0	" 10

The letters heading these columns are those of the preceding table, indicating the per cent of hæmoglobin. It will be seen that 81 per cent of all had at first an index over 1. The reason for this high color index, early supposed to be a characteristic feature of the disease, has been in much dispute. Among the explanations given are: that the cells are overloaded with hæmoglobin that: in this disease the hæmoglobin has a different chemical composition from the normal; there is hæmoglobinæmia; the cells are larger than normal; that hæmoglobinometers are inaccurate; the many microcytes are not counted; the average size of the cells is increased, hence there is increased volume of protoplasm to carry hæmoglobin. We have often blamed the hæmoglobinometers, especially those with a color prism. The lower half of this scale is usually rather incorrectly standardized since the prisms are planed with straight-edges and marked on the assumption that depth of color varies with thickness of the glass. The instruments with one color to standardize, as the Gowers or Sahli instruments, have especial advantages in cases with these low values. But if the error is due to the instruments, then the high indices should occur most frequently in cases with low hæmoglobin values, but a glance at the table on page 55 will show that with hæmoglobin under 30 per cent, 22 cases had an index of 1 or under, 23 over 1, while of the cases with hæmoglobin between 30 and 50 per cent, 21 had an index of 1 or less, 30 over 1.

That microcytes are overlooked in counting cells there is little doubt, and these may contain considerable hæmoglobin. One of our good workers confessed to an error of 200,000 cells in one blood count from this oversight. The evidence that the cells have pigments of an abnormal composition is, we believe, not convincing; also that there is often free hæmoglobin in the plasma which could affect the readings, we doubt. Capps, in his splendid paper, has given good evidence that the high color index is due to the increased size of the cells, not to supersaturation, and the work of Mr. Wroth in this clinic confirms this opinion.

The hæmoglobin line runs almost parallel to that of the red cells. As the case improves the index decreases; towards

death it increases. This is not always the case and sometimes the reverse is true; as for instance of 30 of our cases with improvement, in 7 the index rose, and of 17 cases with an unfavorable course, in 6 it fell. The rule, nevertheless, is that stated above, and it is not uncommon to see an index of 1.1 drop to 0.7 as the count rises, or one of 0.9 rise to even 1.7 before death. These changes may be due either to the newly-formed light-weight cells, or the increasing per cent of large cells, or to several factors.

Leucocytes.—In pernicious anæmia may occur, it is said, a leucopenia or a lymphocytosis. By leucopenia is usually understood a white count of 5000 cells or less. This was true of 74 or 75 per cent of our cases on admission. Of 99 of our admissions the first counts were as follows:

500	to 1,000	2	cases,
1,000	" 3,000	36	"
3,000	" 5,000	36	"
5,000	" 8,000	17	"
8,000	" 10,000	5	"
11,000	" 20,500	3	"

During the course the count varies much, in a lawless manner it would seem, but if one averages a large number of cases, the white count as a rule runs parallel to the red. As a case improves rapidly the leucocytes are high, if slowly, they often remain low. As a case nears the end and all regeneration practically ceases, the reds and whites may fall together.

	Reds.	Leucocytes.	
Case 20.—Nov. 22, '97	1,140,000	2400	
Dec. 1, '97	880,000	3000	
Dec. 4, '97	667,000	666	and death.

During their stay in the hospital 63 of our admissions showed at some time a count of 3000 cells or less. Of these, 41 improved, and 22 died. The counts were as follows:

	Cases which improved.	Which died.
500 to 1,000	1 admission	6 admissions.
1,000 " 2,000	21 admissions	8 "
2,000 " 3,000	19 "	8 "

The above counts occurred during the 63 admissions of 58 patients, of whom 20 or 34 per cent died. The mortality of all our cases with records of leucocyte counts was 32 per cent. Hence a low leucocyte count is not necessarily a bad omen.

The counts within 48 hours of death were as follows:

666	to 1,000	1	case,
1,000	" 3,000	4	cases,
3,000	" 5,000	4	"
5,000	" 8,000	4	"
8,000	" 10,000	2	"
10,000	" 16,000	2	"

Leucocytosis.—For the white cells to rise about 10,000 per cubic millimeter may mean one of several conditions. It may be caused by a complicating acute infection. Thus, of our cases:

Case 1, 12,000 leucocytes, had acute parotitis.
Case 9, 14,440 leucocytes, had pyelonephritis.
Case 43, 12,000 leucocytes, had pulmonary tuberculosis. (This case may also have had a blood crisis.)
Case 63, 12,800 leucocytes, died of a terminal pneumonia.
Case 39, the count of 10,400 white cells may have been due to the dysentery from which he suffered.
Case 65, with 10,300 white cells had fever and abdominal pain.

Or, the leucocytosis may be part of a blood crisis, as in Case 79, with 20,500 cells, and Case 87, with 15,600, both with a normoblastic crisis. Some patients have a terminal (agonal?) leucocytosis. Such patients are very weak, irrational, yet without fever up to the end. Case 24 had 15,200 and Case 80, 16,000 leucocytes. The autopsies did not explain the counts. In other cases no cause can be assigned, as in Case 59 with 12,000 cells. Case 69 is of considerable interest since the cells were high on both admissions, 13,000 on the first and 10,000 on the second. After both admissions the patient improved.

The Differential Count.—In pernicious anæmia especial interest rests in the differential count of the leucocytes. The small mononuclears are said to be increased both relatively and absolutely; the polymorphonuclears to be correspondingly decreased; the eosinophiles to be increased during periods of improvement; and myelocytes are said to be present in unusual numbers. The question at once arises, is there an increased formation of small mononuclears and a decreased formation of neutrophile cells, or do the latter decrease and the former seem actually increased since relatively they are so, while their absolute count remains the same?

The study of our cases convinces us that many processes exist: increased production sometimes, increased destruction (or limited production) in others, while the most important factor is the proportion of the cells, for here more clearly than in any other disease of which we know, is there a tendency for the differential count to remain the same however much the total count may change. That this is not a plasma change is seen by the red-cell counts which change independently of the number of leucocytes.

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.
Case 64.	Oct. 26.....		3,000	28
	Dec. 10.....	2,436,000	5,125	13
	Mar. 21.....	3,508,000	3,000	34
	April 14.....	1,696,000	1,750	37
	May 2.....	1,118,000	4,000	37
	May 17.....	1,668,000	2,250	34
Case 36.	May 22.....	736,000	933	93.6
	June 15.....	513,000	6,000	93.4
Case 39.	May 5.....	1,067,000	3,200	17.3
	June 14.....	1,223,000	2,000	17.7
Case 55.	Oct. 4.....	1,795,000	3,850	40
	Oct. 12.....	1,500,000	4,000	43
	Oct. 18.....	1,800,000	4,250	39
	Nov. 6.....	1,800,000	1,800	46
Case 68.	Aug. 17.....	1,060,000	1,400	28
	Sept. 12.....	1,040,000	1,300	27
	Sept. 30.....	1,760,000	1,600	23
	Oct. 9.....	1,848,000	4,000	26

The same is true even when there is a leucocytosis.

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.	
Case 87.	Mar. 23.....	972,000	3,840	42	
	Mar. 29.....	1,084,000	5,900	35	
	April 2.....	1,368,000	7,380	39	
	April 6.....	1,630,000	15,600	41	
	April 23.....	3,328,000	5,200	38	
Case 63.	Feb. 19.....	1,196,000	4,700	32	
	Mar. 10.....	1,280,000	4,700	32	
	Mar. 18.....		11,000	35	terminal pneumonia
Case 43.	May 3.....	1,850,000	20,500	21	
	May 9.....	1,320,000	8,000	24	
	May 15.....	1,120,000	12,000	22	
	May 22.....	1,325,000	11,500	18	
	June 6.....	1,916,000	5,250	18	
Case 24.	May 11.....	1,300,000	8,800	13	
	May 15.....	1,000,000	15,200	13	
	May 17.....	700,000	11,600	9	

All of these cases show the constancy in the differential count. In other cases the differential count seems to vary with the total count, as if one group of cells was especially involved. In some cases it resembles an inflammatory leucocytosis.

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.
Case 9.	Sept. 30.....	672,000	4,200	26
	Oct. 7.....		14,400	13
Case 80.	Nov. 5.....	1,992,000	3,680	25
	Nov. 20.....	2,040,000	4,280	23
	Dec. 1.....	2,562,000	6,080	47
	Dec. 5.....	1,718,000	4,700	33
	Dec. 8.....	1,874,000	4,000	43
	Dec. 20.....	1,480,000	4,000	43
	Jan. 19.....	1,326,000	16,000	16
Case 69.	Oct. 15.....	1,500,000	10,000	31
	Nov. 21.....	1,328,000	3,000	20

In other cases the rise of small mononuclears is partly absolute but chiefly relative, and explained by the decrease of the granular group:

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.
Case 74.	Feb. 16.....	1,578,000	4,800	54
	Mar. 4.....	1,202,000	2,700	38
	Mar. 30.....	1,012,000	1,250	88
	April 7.....	800,000	950	73
Case 75.	June 20.....	1,760,000	7,500	25
	June 22.....	1,616,000	3,250	37
	July 14.....	880,000	1,200	54
	July 18.....	842,000	1,500	78

Lymphocytosis.—By this term two different conditions are understood. Some mean by it a relative increase of lymphocytes, so that they count over 25 per cent of the whole number; some an absolute increase in these cells to 2000 or more per cubic millimeter. It makes considerable difference which definition is meant, for the percentage may vary greatly while the absolute count remains unchanged if some other group of cells, especially the polymorphonuclear neutrophiles, changes considerably in absolute number. If it is true that these two groups of cells have little relationship (and this is still to be proved), then only an absolute increase can have much meaning. Since the personal element is a very strong factor in separating the small mononuclears from large mononuclears and transitionals, and since in this disease the separation of these groups is not so very important, we prefer to group them all under the heading "mononuclear nongranulars" or "basophiles" and consider 30 per cent the normal percentage and 2500 the normal absolute number.

An absolute lymphocytosis (over 2500 mononuclear nongranulars) occurred at some time during the course of 18 of 69 cases. Of these 11 died, a mortality of 61 per cent. Hence the presence of this condition seems unfavorable. It often exists just before death. These counts were, from

2500 to 3000..... 7 cases,
3000 " 3500..... 6 "
3500 " 5000..... 4 "
5580 ..... 1 case at death.

In these cases the percentages of these mononuclear nongranular cells at the time of the above absolute numbers were, from

10 to 30%..... 4 cases,
30 " 40%..... 5 "
40 " 60%..... 6 "
70 " 80%..... 2 "
93.4% ..... 1 case at death,

and the total leucocyte counts, from

4,000 to 6,000..... 4 cases,
6,000 " 10,000..... 10 "
over 10,000..... 4 "

The highest leucocyte count was 20,500, of which 21.4 per cent, or 4380, were mononuclear nongranular cells.

In case the total leucocyte count is only 3000 cells or fewer it is clear that an absolute lymphocytosis cannot exist, but it is interesting to see how many of these few cells were mononuclear nongranulars. Some time during their course 39 of our cases (with good blood records) had a total white count of 3000 or fewer. Of these the percentage of mononuclear nongranulars was in

16 cases between 30 and 40%,
10 " " 40 " 50%,

The lowest percentages were, 10.3 per cent when the total leucocyte count was 1800 cells; 16 per cent when the total leucocyte count was 1320 cells; and 17.7 per cent when the leucocyte count was 2000 cells. In 4 cases the percentages of mononuclear nongranular cells was 70 or over, and the total leucocyte counts 1500 cells or under.

A relative lymphocytosis, that is, a percentage of mononuclear nongranular cells of 30 or over, occurred in all but 6 of 69 cases. Hence there was a relative lymphocytosis in 91

per cent of our cases, an absolute in 26 per cent. Since, however, the total leucocyte counts tend to run low in this disease we must conclude that an increase in the absolute number is commonly the rule.

Eosinophilia.—The behavior of the eosinophile cells has attracted much attention since their number is believed to be an index of marrow activity. As these cells seem to bear no direct relation to other cells it is their absolute number which is important; over 250 per cubic millimeter means an increase beyond physiological limits. A percentage of over 4 usually means an eosinophilia, but not always. An increase in these cells usually accompanies a rapid increase in the red cells, but often a slow one, while towards the end their high number may be proof of energetic but unsuccessful attempts of the marrow to replenish the blood. Their increase is a common feature of a blood crisis (see page 58).

In 17 of our cases these cells rose with the red cells, and in 10 cases fell with them. The total disappearance of these cells is a bad sign.

	Date.	Reds.	Leucocytes.	Percentage of eosinophiles.
Case 24.	May 11	1,300,000	8,800	1.6%
	13	1,100,000	9,000	0
	15	1,000,000	15,200	0
	17	700,000	11,600	0
	18	637,000	9,200	death.

The disappearance of these cells may be a valuable sign in cases in which the reds are not falling.

	Date.	Reds.	Leucocytes.	Percentage of eosinophiles.
Case 60.	July 22	2,832,000	5,200	
	23	2,769,000	3,400	5.4%
	27	2,568,000		
	30	2,888,000	4,500	4.0%
	Aug. 3	2,672,000	5,500	
	6	2,704,000	4,000	
	7	death.		

A true eosinophilia occurred in 11 cases, 3 of whom died. The count of the eosinophile cells was:

250 to 300	2 cases,
300 " 400	3 "
400 " 500	4 "
630 " 858	4 "

while these cells were of the total leucocyte count, from

3 to 4.0%	1 case,
4 " 5.0%	2 cases,
6.3 " 9.2%	6 "
14.7 and 15.6%	2 "

In 5 cases the red cells were rising, while the eosinophile count was high; in 5 they were not rising; in one case the point was not determined. In 3 cases the eosinophile count was highest on admission.

The behavior of these cells in a case during improvement is well illustrated by the following:

	Date.	Reds.	Leucocytes.	Eosinophile per cent.	Eosinophile count.
Case 51.	Oct. 8	1,892,000	4,250		
	9		3,500	2.4	84
	11	1,921,000	2,500	5.4	135
	21	1,788,000	3,700		
	31	2,000,000	2,500		
	Nov. 4	1,608,000	2,000		
	14	1,800,000	1,600		
	22	2,860,000	1,200		
	Dec. 5	2,850,000	5,000	7.5	375
	7	3,424,000	3,800	5.5	210
	12	3,600,000	5,300	3.3	175
	19	3,508,000	5,100	3.7	190
	26	3,624,000	5,000	7.6	380
	Jan. 1	3,600,000	6,500	4.0	260
	9	3,952,000	7,500	5.0	375
	15	3,804,000	6,700	3.7	350
	23	3,532,000	6,000	3.3	198
	30	3,604,000	5,000	3.3	165
	Feb. 6	2,600,000	4,150	5.0	208
	19	2,500,000	3,600	7.1	256
	20	2,900,000	2,800	6.2	173
	27	3,000,000	2,400	7.0	168
	Mar. 6	3,100,000	2,100	14.75	315
	13	3,740,000	3,700	9.8	349
	20	3,848,000	3,700	6.3	233
	27	3,872,000	6,200	6.8	422
	April 3	3,820,000	6,000	4.3	258
	11	4,208,000	8,000	3.8	304
	17	4,302,000	6,500	2.3	150

A *relative eosinophilia* (over 4 per cent), the above cases not included, occurred in 15 cases. Four of these died. Of these 15 cases, in 3 the reds were rising at the time the percentage of eosinophiles was high, in 6 they were not rising, in 5 they were falling, and in one it was doubtful. These percentages were from

4 to 5%	4 cases,
5 " 6%	4 "
6 " 7%	3 "
7 " 8%	2 "
9 " 10%	2 "

and the total leucocyte counts were

1,000	1 case,
1,000 to 2,000	5 cases,
2,000 " 3,000	4 "
3,000 " 4,000	4 "
5,000	1 "

While a rise of the eosinophile cells may mean increased marrow activity, it certainly does not always mean that the prognosis is good.

Myelocytes occur more constantly and in greater numbers in pernicious anæmia than in any other disease except leukæmia. In 28 of our cases they were present in numbers varying from 0.2 to 0.8 per cent ,and in the majority of these from 0.4 to 0.8 per cent.

Blood Crises.—A blood crisis may be defined as a period during which large numbers of nucleated reds are present in the peripheral blood. v. Noorden thought that they occurred while the bone-marrow was especially active in the formation

of red cells, and that they were followed by a jump in the red-cell count. The leucocytes, especially the eosinophiles, should also rise. While in cases of chlorosis and of secondary anæmia blood crises may be evidence of improvement, in pernicious anæmia this is by no means always the case. The most strenuous attempts of the exhausted bone-marrow to stem the tide of blood destruction may be fruitless, and the remarkable display of nucleated reds and leucocytes in the blood may be described as analogous to the muscular convulsions preceding death.

An arbitrary line must of course be drawn to define a blood crisis. That which seemed most natural, judged by our cases, was 50 or more nucleated reds per 1000 leucocytes. Accepting this number as a limit, blood crises occurred in 14 of 70 cases.

There are two kinds of blood crises, and seldom is there doubt in this classification: the normoblastic and the megaloblastic. They are classified according to the predominating nucleated red cell. Intermediate cells are here counted as megaloblasts. By normoblastic crisis is meant a period during which there are present in the circulating blood 50 or over nucleated reds per 1000 leucocytes, and the majority of which nucleated reds are normoblasts. This occurred in 5 of our cases. The nucleated cells varied:

normoblasts	.....from	192	to	5896	per 1000 leucocytes,
intermediates	..... "	0	"	112	" 1000 "
megaloblasts	..... "	0	"	161	" 1000 "

Four of these accompanied a rising red count. In the fifth the reds remained constant.

	Date.	Reds.	Leucocytes.	Normoblasts per cubic millimeter.
Case 10.	April 18....	1,792,000	11,750	5,896
	May 5....	2,720,000	20,500	

			(Per 100 leucocytes.)				
	Date.	Red.	Normoblasts.	Intermediates.	Megaloblasts.	Leucocytes.	Eosinophile per cent.
Case 10.	Mar. 29	1,084,000	16	14	12	5,900	2.6%
	April 2	1,368,000	106	62	101	7,280	3.0%
	6	1,630,000	1064	112	8	15,600	5.5%
	16	2,887,000	0	0	2	5,320	8.5%
	23	3,328,000	0	2	0	5,200	14.0%
	May 3	3,672,000					

This is a complete crisis, with the many nucleated reds, the leucocytosis, the eosinophilia, and the good result.

There were 9 megaloblastic crises. The cells varied as follows:

normoblasts	.....	10	to	1400	
intermediates	.....	0	"	460	
megaloblasts	.....	36	"	240	per 1000 leucocytes.

During 7 of these there was a fall in the red count, in 2 a slight gain. The difference in the efficiency of normoblastic and megaloblastic crises is very evident.

The leucocytes during these crises numbered from

1,000	to	2,000.....	3 cases,
2,000	"	3,000.....	4 "
3,000	"	7,000.....	5 "
11,750	and	15,600.....	2 "

Even the greatest crisis may not be efficient. In Case 80 the crisis continued 19 weeks. The reds first rose from 1,902,000 to 2,562,000, and then fell to 1,328,000 at death. The leucocytes varied from 3000 to 5000 till death when the count was 16,000. The normoblasts were always above 500 per 1000 leucocytes. On one day there were 14,388 normoblasts, 460 intermediates, 138 megaloblasts, and 239 microblasts per cubic millimeter. This was shortly before death while the total red count was falling.

A NOTE ON THE VOLUME AND COLOR INDEX OF THE RED CORPUSCLES.

By PEREGRINE WROTH, JR., M. D.

(From the Medical Clinic of The Johns Hopkins Hospital.)

In an article, entitled "A Study of Volume Index," published in "The Journal of Medical Research" for December, 1903, Dr. Joseph A. Capps, of Rush Medical College, described the relation existing between the hæmoglobin content and the cubic contents of red cells in various diseases. His exhaustive study of 175 cases, including all kinds of anæmias, in all stages of progress, leaves nothing new to be said, but at the suggestion of Dr. Emerson 11 cases of anæmia which have been in our wards this spring have been studied in the same manner in which Dr. Capps studied his cases.

The points made by Dr. Capps which come out most clearly in the following cases are these:

(1) In primary anæmias the cell volume is increased.

(2) In secondary anæmias the cell volume is decreased.

(3) Red cells do not become supersaturated with Hb., that is the increase in Hb. content never exceeds the increase in cell volume; but on the other hand in secondary anæmias the decrease in Hb. content may be more marked than the diminution in the size of the cell.

In the cases studied the following method was used:

(1) The number of red cells per cubic millimeter was determined in the usual way.

(2) The Hb. percentage was determined in the first 6 cases by the Sahli hæmometer and the reading corrected so as to correspond to the standard Miescher in use here. In the last 5 cases the Miescher instrument was used directly, 14 g. of Hb. per 100 cc. being taken as 100 per cent.

(3) The volume of the cells was determined by the hæma-

tocrit, fresh blood, undiluted by any fixing fluid, being used, and the machine rotated for at least four minutes, 50.3° on the scale, Daland's latest figures, being taken as the reading for 5,000,000 normal cells.

(4) The diameter of the individual cell represents the average of 150 measurements made with an eye-piece micrometer which had been standardized before using. The cells were measured in the fresh state. No crenated cells or cells showing shapes not approximately normal were included.

(5) The thickness of the cell and the cubic contents of the individual cell were calculated from the reading on the hæmatocrit, the number of red cells, and the average diameter. These figures thus are not actual measurements, but merely percentages, the normal thickness being considered 1.00, and the normal cubic contents 1.00.

(6) The color index is the quotient obtained by dividing the Hb. per cent by the percentage of red cells per cubic millimeter, 5,000,000 red cells of course being 100 per cent.

(7) The volume index, a term proposed by Capps, is "the percentage volume of red cells (determined by the hæmatocrit) divided by the percentage number of cells. This will give the percentage volume of the individual cell.

(8) The surface, as I have called it here, is not the surface of the red cell in square microns, but merely the percentage surface, the surface of the normal cell being considered 1.00.

In Cases I, II, and III, the hæmatocrit was not used.

Case	No. of reds.	Hb.	C. I.	V. I.	Hæmat.	Diam.	Surface.	Thick.	Cu. Cont.	G. per 100 cc.	New C. I.
I.	4,836,000	87	.9	....	....	7.31μ	.94	....	....		
II.	2,358,000	69	1.46	....	...	8.85μ	1.39	....	....		
III.	1,644,000	49	1.5	....	....	8.69μ	1.34	....	....		
IV.	1,756,000	16	.45	.56	10	6.7 μ	.79	.7	.56		
V.	4,424,000	71	.806	.85	38	7.76μ	1.07	.8	.85		
VI.	3,840,000	33.5	.44	.48	18.8	6.9 μ	.84	.58	48		
VII.	4,636,000	55.4	.59	.73	34.5	6.81μ	.82	.9	.73	7.76	.64
VIII.	4,072,000	69.5	.85	.804	32.9	7.68μ	1.02	.789	.804	9.73	.92
IX.	3,820,000	39.2	.51	.59	22.7	7.08μ	.89	.66	.587	5.49	.54
X.	2,552,000	59.8	1.10	1.12	29.07	9.08μ	1.46	.77	1.12	8.37	1.27
XI.	800,000	16	1.00	1.04	8.4	8.6 μ	1.31	.79	1.04	2.25	1.07

Case I.—Practically normal. Cell a trifle small, C. I. correspondingly decreased.

Cases II and III.—Cases of pernicious anæmia. The C. I. is high, that is, the Hb. content of the cell is greater than normal, but at the same time with the increased diameter as shown by measurement the surface is increased to almost as great an extent as the Hb. content.

Case X.—Also a case of primary anæmia. (In this and the following cases the hæmatocrit was used.)

The following points are clear:

(1) The cell diameter is increased considerably more than Hb. content.

(2) The cell thickness is decreased.

(3) Volume index is greater than color index, that is the cell has increased more in size than it has in Hb. content. In other words, though the Hb. content is increased the cell is not supersaturated with Hb.

Case XI.—Clinically a case of pernicious anæmia, though the color index is just 1.00. In this case with Hb. content at normal, the size of the cell has increased. This might be taken as confirming Capps' statement that the volume index is a more trustworthy guide than the color index, as to whether we are dealing with a primary or secondary anæmia.

Cases V and VIII.—These are secondary anæmias.

The following points are made out:

(1) Low color index.

(2) Cell diameter greater than normal.

(3) But thickness of cell has decreased to such an extent that

(4) Cubic contents (volume index) is less than normal, and corresponds very closely to the value expressed by the low color index.

Here then are two cases of secondary anæmia, in which with a low color index, we have a cell which as seen under the microscope appears larger than normal, the decrease in volume being due to the great decrease in thickness.

In Cases IV, VI, and IX, the anæmia is of the secondary type, and the cell is decreased both in diameter and thickness. The decrease in volume as shown by the volume index is practically the same as the decrease in Hb. content as shown by the color index.

Case XI is a case of secondary anæmia which bears out Capps' statement that the decrease in Hb. content often exceeds the decrease in volume, that is, the cell lacks considerably being saturated with Hb.

In only one case in the series is there a suggestion of supersaturation with Hb., Case VIII, one of the secondary anæmias.

As said before, in Cases VII to XI inclusive, the Hb. was calculated in grammes per 100 cc. and it is therefore possible to compare the new color index proposed by Dr. Emerson with the volume index as determined by the hæmatocrit.

This new color index is determined by dividing, in any given case, the "grammes per million" by the factor 2.63, this factor being the normal "grammes per million." By referring to the table it will be seen that in every case the new color index is higher than the old color index, and in three cases (VII, X, and XI) is considerably higher than the volume index. This difference is due to the fact that in the first calculations 14 g. of Hb. per 100 cc. was taken as the normal, while in the determination of the new color index 13.15 g. of Hb. per 100 cc., a quantity which Dr. Emerson has found to be more nearly correct for the normal person, has been taken for 100 per cent.

Judged simply by these few cases it would seem that a cell can be supersaturated with Hb., but of course it will require a great number of observations on the relation between the volume index and the new color index before anything definite can be said.

PULSATING EMPYEMA.

By W. J. Calvert, *Columbia, Mo.*

In this second paper on pulsating empyema,[1] I wish to reconsider some factors of the subject in the light of some experimental work recently done by myself in Dr. C. W. Green's Physiological Laboratory.

Experiment.—A cannula connected with a mercury manometer was inserted in the right carotid artery. A cannula connected with a mercury manometer and a large bottle of normal salt solution was inserted in the pericardium. From the bottle, salt solution was allowed to flow into the pericardium under varying pressures and the intra-pericardial pressures and pericardial pulsations were recorded along with the pulse.

This experiment demonstrated that, when the pericardium is distended with fluid, there is a pericardial pulsation with each heart cycle. The tracings show that as the pulse curve rises the pericardial curve falls. When the pulse curve is highest the pericardial curve is lowest and as the pulse curve falls the pericardial curve rises. The pulsation of the pericardium which is diastolic in time is caused by the diminution in the size of the heart during systole and directly to the blood leaving the heart. As a portion of the blood leaving the left ventricle passes out of the thorax to the head and arms, the amount of blood passing through the thoracic aorta is less than the contents of the left ventricle. (The blood in the right ventricle remaining within the thorax may be disregarded.) The end result is that the thoracic contents are diminished in systole by the heart's contraction and increased by the distension of the aorta. The distension of the aorta in systole cannot compensate for the diminution in the size of the heart because a portion of the blood passes immediately out of the thorax to the head and arms and out of the thoracic into the abdominal aorta. (The amount of blood flowing into the thorax through the large veins in this short interval of time is of very little practical importance in this consideration.)

The thoracic cavity becomes smaller during systole by the amount of blood which leaves the cavity. If under normal conditions a pulsation occurs it should be diastolic in time, as is true of the pericardium, and for the same reasons.

In pleurisy and empyema the factors necessary to produce a pulsation of the thoracic wall are as follows: a firmly fixed pulsating organ; contact of the pleural wall with this pulsating organ; distension of the pleural sac with fluid, air, or solid material, and collapsed condition of the lung. The first requirement is fulfilled by the thoracic aorta; the second, by the normal relationship of pleural wall to thoracic aorta; the third, by presence of fluid, pus, or a combination of these with air in the pleural cavity; and the fourth, by the collapsed condition of the lung in pleurisy and empyema. With each increment of pressure the weakest portion of the wall will expand first.

As a direct factor in causing the pulsation the heart may be excluded or else the pulsation must be diastolic in time. The sudden flow of blood into the aorta causes the vessel to suddenly become larger or to pulsate.

The intra-pleural pressure must be sufficiently great to stretch the pleural wall to a degree which will permit them to take up the systolic diminution in the size of the thorax and remain sufficiently taut to respond to the sudden increase in size of the thoracic aorta, or to manifest a systolic pulsation synchronous with the pulsation of the aorta. When the weakest portion of the pleural wall is external that portion must pulsate.

The right ventricle forces a certain amount of blood into the compressed lung which must be larger during systole and consequently add a minor factor to the intra-pleural pressure and consequently to the systolic pulsation.

The anatomical relationship of the aorta to the right and left pleura has been previously described and accounts for the frequency of left-sided pulsating pleurisy and empyema.

Dr. Sailer[2] has reviewed in detail the literature, to 1904, on pulsations of the thoracic walls and their causes.

[1] W. J. Calvert, "The Cause of Pulsation in Empyema." The Am. J. Med. Sciences, Nov., 1905, p. 890.

[2] Joseph Sailer, "A Study of Circumscribed and Diffuse Pulsation of the Wall of the Thorax." The American Journal of Medical Sciences, August, 1904.

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LETTER FROM CAMPBELL P. HOWARD, M. D.

BERLIN, NOVEMBER 21, 1906.

To the Editor of The Johns Hopkins Hospital Bulletin, Baltimore, Md., U. S. A.

DEAR SIR:—Professors Welch, of Baltimore, and Blackader, of Montreal, suggested that a letter to your journal concerning "the Medical Advantages of Munich," might prove of interest to your readers. First as to Munich itself. There is scarcely any city in Europe, that has so many attractions for a visitor as Munich, situated as it is in the beautiful valley of the Isar, within sight of the snow-capped Bavarian Alps and easy access of endless excursions. Art flourishes in Munich, as evidenced by the picture galleries, which contain some of the most celebrated paintings in Europe, and by the music, which is excellent—the opera being second only to that of Wien. The rate of living is moderate, the pensions numerous and for the most part comfortable, the people polite, sympathetic and (to use a favorite expression of their own)—*gemütlich*. Lastly, for one who has yet to learn the language, Munich has exceptional advantages, because the English-speaking people are not so numerous that one cannot escape them (a statement which cannot be made of Berlin or Wien); hence one can, if one so desires, associate with a German-speaking "Kreis." Yet one is in a city of nearly 600,000 people, with good theaters, concerts, art galleries, and other diversions for the home-sick "Ausländer."

As to medicine. The "Königliche Ludwig-Maximilians Universität" has a medical faculty of which it has a just right to feel proud, and one that lives up to the high standards set by its former teachers—Pettenkofer, Ziemsen, etc. It includes at present such men as Voit, in physiology; Rückert, in anatomy; Bollinger and Dürck, in pathology; Gruber, in hygiene; Angerer, in general surgery; Lange, in orthopedics; Winckel, in gynæcology and obstetrics; Bauer, Müller, and May, in medicine; and Kraepelin, in psychiatry. For the "course-crazed" student Munich offers no facilities when compared with Berlin or Wien, but one can occupy his day very well with a schedule, which would include the majority of the above-mentioned teachers.

It is especially to those interested in internal medicine that Munich is to be highly recommended. For one who has just graduated from the medical school, but above all for one who, having served two or three years as an "Interne" in a general hospital, wishes to specialize in internal medicine, Munich is the place "par excellence." In the morning he can hear lectures on morbid anatomy by Bollinger and Dürck, attend the theater clinic of Friederich Müller, work in the poliklinik with May, and in the afternoon study psychiatry with Kraepelin.

A man, who has a moderately good training and speaks and writes German, may procure a "Volontärship" in the wards of Professor Müller, the value of which can only be realized by a visit to the two hundred and fifty public beds, which comprise the service of the "second klinik." If one does not write and speak German sufficiently fluently or does not wish to do "clinical routine," one can obtain work in the laboratory, where, under the guidance of Professor Müller and his assistants, an original "Arbeit" in chemistry, bacteriology, or pathological histology may be undertaken. Professor Müller has surrounded himself with an unusually capable group of assistants, each of whom is a specialist in some experimental line of work, and, therefore, best fitted to investigate certain series of cases. Naturally the room in the laboratory is limited, and a man desiring such work must satisfy Professor Müller as to his qualifications and undertake to stay a definite length of time (three to six months).

A word as to Müller as a teacher. He ranks among the first three men in clinical medicine in Germany and is considered by many the best teacher. His lectures are simple, thorough, and painstaking. His cases are carefully prepared and honestly presented, and a student, no matter how advanced, never leaves his lecture-room without having acquired some new fact or thought, even though the text be a time-worn one, as typhoid or pneumonia. He is an inspiring teacher, a practical physician, and a scientist in the best sense of the term. His great interest in the chemical side of medicine is especially stimulating, and his lectures on the diseases of metabolism are most instructive. By the teacher of clinical medicine his methods of teaching are well worth careful consideration and imitation, and a visit of a week or two in his klinik will never be regretted.

Hoping that this letter will prove of assistance to some of your readers, who, wishing to spend "a year abroad," are undecided as to the choice of the klinik, and thanking you for so much of your valuable space. Believe me,

Yours truly,

CAMPBELL P. HOWARD.

SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL OR MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

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——— Report of Some Surgical Cases Treated at the James Walker Memorial Hospital, Wilmington, N. C.—*Ibid.*

AMBERG, S., M. D. A Method for the Determination of Hydrogen Peroxide in Milk, together with Some Observations on the Preservation of Milk by this Substance.—*The Journal of Biological Chemistry,* Vol. I, Nos. 2-3, 1906.

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STUDIES IN GENITO-URINARY SURGERY

The Johns Hopkins Hospital Reports, Volumes XIII and XIV, will be issued in January, 1907. Volume XIII will consist of about 605 pages with 201 figures in the text, six plates and one colored chart.

Volume XIV will consist of about 632 pages, and have 97 figures in the text.

The price of each volume will be five dollars ($5.00), bound in paper, and five dollars and fifty cents ($5.50), bound in cloth.

Remittances and orders will now be received.

THE JOHNS HOPKINS PRESS, BALTIMORE, MD.

NOTES ON NEW BOOKS.

The Physicians' Visiting List. (*Philadelphia: P. Blakiston's Son & Co., 1907.*)

This small pocket note-book is a useful one for any doctor; it is well arranged, beginning with a calendar for 1907-1908; it contains tables of incompatibility, of antidotes and doses, etc.; followed by a visiting list with special memoranda for 25 patients per week. In all senses it is handy and helpful.

Review of the Practice of Gynecology. By DR. J. W. BOVEE. (Lea Brothers & Co., Philadelphia and New York, 1906.)

It may be true that Gynecology as a specialty is "passing," but the number of new books each year and new editions of older works devoted to this branch of surgery indicates that it still has no small degree of vitality. A recent addition to the literature is the Practice of Gynecology, edited by Dr. J. W. Bovee. This work is a collaboration by American authors. It is intended chiefly for the general practitioner, and omits, therefore, much of interest to the specialist. It includes chapters on diseases of all of the pelvic organs, as well as the ureters and kidneys in the female, thus treating more than formerly belonged to the province of the gynecologist.

The book as a whole is well written, well illustrated, clear and complete. It has some of the faults which are difficult to avoid in a collaboration. The arrangement of the chapters is not logical, urinary fistula coming early, after displacements of the uterus, and diseases of the rectum and anus being introduced between diseases of the vagina and inflammations of the uterus. There is some repetition. Two pictures of Fowler's position are unnecessary, as are also two detailed descriptions of vaginal hysterectomy, with plates. Prolapse of the uterus scarcely receives the attention it deserves.

There are numerous excellent chapters, of which those on examinations, inflammations of the uterus, fibro-myomata of the uterus, infections of the tubes and ovaries, and extra-uterine pregnancy, are especially good.

In regard to radical operation for malignant disease of the uterus, the writer takes a wise middle position suitable for a text-book. The author of the vaginal method of operating, while presenting the subject well, writes as an advocate and does not give impartial views. The chapter on post-operative treatment and complications of abdominal operations dismisses renal complications as "of frequent occurrence. Indeed the function of no organ demands more careful and constant attention after operation than the kidney." Three lines are, however, adequate. Cystitis is better. It receives six lines (see page 530).

The index is good and the press work of the usual high standard of the publishers.

Progressive Medicine. Vol. III. September, 1906. Section on Obstetrics. (*Philadelphia and New York: Lea Brothers & Co., 1906.*)

This review of the year's work in Obstetrics covers one hundred pages and is based on seventy-five papers of which eleven are from the French and the Italian, while the remainder are about equally divided between German and English publications (including American). Among the periodicals of this country the clippings from the New York Medical Journal have a noticeable predominance.

The literature on "The Toxæmia of Pregnancy" is exclusively represented by massive quotations from two papers. One of these "On the Chemistry of Toxæmias of Pregnancy" is purely theoretical and has for its chief purpose the undermining of a suggestion by Williams that the ammonia coefficient of the urine may be taken as a guide in differentiating the grave cases of vomiting of pregnancy. The method has been in practical use in the obstetrical clinic of the Johns Hopkins Hospital for three years and remains the most reliable means we possess for determining where an abortion is necessary and where it is not. Wolf's quoted opinion that the ammonia variation in these cases depends on the patient's weight is not in accord with the facts and consequently his deductions are valueless.

The only other contribution of the year to toxæmia which the reviewer regards worthy of mention is Edgar's "Clinical Manifestations." In this a futile effort is made to classify toxæmias according to symptoms. Clearly, no logical classification is possible save that in which the pathological lesions are taken as criteria. It naturally follows that Edgar's papers add confusion to the subject of toxæmia of pregnancy and represent a backward rather than a progressive trend.

Undue space and prominence is often given to ludicrous therapeutic suggestions. Two pages are occupied with the report of a case of eclampsia in which recovery has followed the use of copious enemata of milk sugar. Again, a detailed account of Koplinski's view of the value of pork in treating the vomiting of pregnancy is quoted. This style of diet is recommended, because it is so heavy "that ejection from the stomach is wellnigh impossible."

The section on "Obstetric Surgery" is the most satisfactory portion of the review. The citations here give a fair idea of the contention which exists regarding the relative merits of vaginal Cæsarean section and dilatation of the cervix with the instrument of Bossi, though it is not made clear to the reader that the weight of authority and experience is in favor of the cutting operation.

Pubiotomy is duly credited with a steady increase in popularity. The gain in length of the various diameters of the pelvis, the anatomical relations of the site of operation, and the prevailing technique in its execution are discussed in the light of recent contributions.

The section on "The Puerperal Period" relates almost altogether to the bacteriology of the uterus after delivery in normal as well as in infected cases. A continued lack of agreement is shown with regard to many practical points, such as, the advisability of the antepartum douche, the possibility of auto-infection, and the proper therapeutic measures when infection has occurred. The review points no distinct advance in these problems during the past year and is characterised by an indecisiveness that we feel is unfortunate. The practitioner is left in grave doubt where sound wisdom could be supplied, if the reviewer would give more space to monographs founded on careful and conscientious work, eliminating ridiculous papers and such as lack the ear-marks of honest laboratory experiment or clear-minded clinical observations.

J. MORRIS SLEMONS.

The Nervous System of Vertebrates. By J. B. JOHNSTON, PH. D., Professor of Zoology in West Virginia University. Pp. I-XX + 370, with 180 illustrations. Price $3. (*Philadelphia: P. Blakiston's Son & Co., 1906.*)

This book will be read with much eagerness by those who feel dissatisfied with the customary cumbersome method of presenting the comparative anatomy of the nervous system. It is an outgrowth of previous papers by the same author, and consists of a description of the vertebrate nervous system based on its functional analysis. Under the influence of Gaskell he divides the brain and cord into four primary longitudinal systems, and uses them as units of description. The success which he has had in demonstrating the fundamental character of these units indicates the possibility of the introduction of such a basis of analysis into general use.

There are those who may not agree with him in some of his interpretations; as for instance, where (p. 328), he attributes the degeneration of the forward end of the hippocampus in higher vertebrates to the growth of the corpus callosum; others might say that the rudimentary hippocampus was the result of a rudimentary olfactory end-organ, and that the presence of the corpus callosum was an unrelated coincidence. Also some will disagree with him where (p. 176) he classifies the olfactory apparatus under the visceral sensory system, instead of placing it, like the optic apparatus, under the modified cutaneous or somatic sensory system. Under the neurone theory he omits the cell-chain hypothesis of fiber formation, and what is more important makes no mention of Harrison's experiments on the histogenesis of nerve fibers. All through the text there is scant reference made to authorities. This is to be regretted inasmuch as the author is apparently thoroughly familiar with the literature and it would have been of great convenience to the reader. Such things of course are only details, the real thing to be considered is the fact that the author has given us a new presentation of the whole vertebrate nervous system which not only portrays its essential morphology, but does this in terms of function, consistent with a living mechanism. G. L. S.

A Practical Treatise on Fractures and Dislocations. By Lewis A. Stimson, B. A., M. D., LL.D., Professor of Surgery in Cornell University Medical School, etc. Fourth edition. Revised and enlarged. (*New York and Philadelphia: Lea Brothers & Co., 1905.*)

The fact that this work has passed through four editions testifies to its popularity and worth.

Since the last edition, the very general use of the X-ray and the frequent use of the open operation have contributed a great deal to our knowledge of fractures, especially those into and near the joints. In the revision of his book, the author has made full use of the knowledge thus acquired. The chapters dealing with fractures and dislocations of the carpal bones and fractures of the lower end of the humerus in children have been largely rewritten.

A large number of skiagrams have been added, which increase the value and attractiveness of the volume.

Essentials of Human Physiology. By D. Noël Paton, M. D., etc. Second edition, revised and enlarged. (*Chicago: W. T. Keener & Co., 1905.*)

According to the preface the object of this work is to put into the hands of medical students a volume emphasizing those parts of physiology which are of special interest and importance to the future practitioner. In the execution of this worthy intention the author has not been markedly successful.

It is to be regretted that no distinction should have been drawn between systolic and diastolic blood pressures and that the author should have confined himself to the bold assertion that the Hill-Recklinghausen instrument may be used for the determination of the blood-pressure in man (p. 258). The truth of many of the author's statements might be called into question as for instance where it is affirmed that the absence of the pulse in the veins is due to the low resistance offered to the passage of the blood toward the heart (p. 247), or where one reads that the vagus is "a true excito-motor nerve of the respiratory center" and is stimulated only during collapse of the lungs (p. 293).

Sometimes an incomplete account is as bad as one which is frankly incorrect as for instance the treatment of venous pulsations (p. 255), and of sleep (p. 177). Now the reader is tempted to ask how the contracting heart pulls upon the lungs in order to produce the cardio-pneumatic movements (p. 297), and again to wonder at the remark that there is no evidence in favor of the neurogenic hypothesis of cardiac contraction (p. 238).

If a text-book cannot be original it may at least be well written, accurate and, as far as it goes, complete. It is unfortunate that the work in question has none of these qualities.

Percy M. Dawson.

An Introduction to Physiology. By William Townsend Porter, M. D., Associate Professor of Physiology in the Harvard Medical School. (*Philadelphia and London: J. B. Lippincott Company, 1906.*)

Those who are concerned with the science of education cannot afford to be ignorant of the opinions of Professor Porter. According to Professor Porter physiology should be taught in the laboratory by means of experiments performed by the student himself. These experiments should not be performed for the purpose of clearing up notions gained from books and lectures, but on the contrary they should be regarded as of primary importance and serve as the point of departure for such reading as may be necessary for their explanation and correlation. The method of Professor Porter may be of questionable value in handling large classes, but if so it is possible that all other methods which really teach anything are open to the same objection.

The Introduction to Physiology is an excellent expression of the author's views. It is therefore not an ordinary laboratory manual. Its aim is not only to give directions for a long series of feasible and important practical exercises, but to explain and discuss (sometimes with references to the original literature) the methods and apparatus employed and the results obtained. The seventy-four illustrations are simple in character, but clear and well chosen. It is to be regretted that there are no chapters on mammalian vivisection, a branch of physiology of the greatest importance to medical students. This is, however, the fault not of the author but of the antivivisectionists who, with the best intentions, are limiting the efficiency of medical education in some sections of the country.

Those who are of Professor Porter's way of thinking will see in the introduction an epoch-making work; while those who do not agree with him will nevertheless find it an extensive, very helpful and well written laboratory guide.

Percy M. Dawson.

The Thirteenth Annual Report of the Craig Colony for Epileptics. By Dr. William P. Spratling. Sonyea, N. Y.

The Thirteenth Annual Report of the Craig Colony for Epileptics just issued contains 106 pages. It is profusely illustrated in a way to show all sides of colony life.

The Colony embraces 1695 acres of land, comprises at present 76 houses, with six more going up for 200 additional patients. The present census is nearly 1300 all told; when the new buildings are completed the total census will be approximately 1500. There are now about 1000 epileptics in the State who cannot be received, because there is no room.

A new departure in Dr. Spratling's report this year is a special section devoted to scientific papers and reports made up of articles contributed by members of the medical staff. That the amount of surgical work alone performed at Sonyea is considerable, is shown by the fact that anæsthetics for surgical purposes were given 172 times during the year.

A modern hydrotherapeutic plant after the plans of Dr. Baruch has been installed and the plant has been a valuable feature in the treatment of certain types of epilepsy.

The net per capita cost of keeping each patient at the Colony last year was $141.38. We believe this is about $35 a year less than keeping an insane person in a State Hospital for the insane.

There is a movement on foot initiated at the Colony to establish a second Colony for epileptics nearer New York City.

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ACUTE LEUKÆMIA.

By Charles P. Emerson, M. D.,

Associate in Medicine, The Johns Hopkins University; Resident Physician, The Johns Hopkins Hospital.

During the past year three cases of so-called acute leukæmia have been treated in the medical wards of the Johns Hopkins Hospital. These have been of so much interest, and have presented certain features of such unusual nature that it is thought to be of value to report them.

Case I.—*A case of acute lymphatic leukæmia without enlargement of lymph glands or spleen, with localized involvement of the bone-marrow, and with very many white cells soluble in dilute acetic acid.*

W. A. C.; age 35 years; male; white; Gen. No. 52738. Admitted Oct. 30, 1905. Died Nov. 1, 1905. Clinical diagnosis: Acute lymphatic leukæmia.

The patient came complaining of "weakness."

His family history was negative, except that his father was a heavy drinker.

The past history was also negative, since he claimed to have "always enjoyed good health." He has had measles, mumps, and whooping cough. He denied having had typhoid fever, pneumonia, rheumatism, pleurisy, scarlet fever, chronic cough, stomach trouble, or any urinary disturbance. He admitted gonorrhœa, buboes, chancre, but denied all secondaries. His work kept him out of doors most of the time. He was usually a little constipated. He took an "occasional drink," but not one every day.

Present illness.—The patient said this began insidiously, and was first noticed September 1 of this year (just eight weeks ago). He first noticed weakness, hence, taking September for his vacation, he went on a pleasure trip during which he became much worse and was in bed one week because of the weakness, his one symptom. Since then he tired very easily, was dyspneic on exertion, but had no pain, no nausea, and no vomiting. He had slight constipation; his appetite was fair. He was not pale, had no swollen glands, no increased micturition, no swelling of the feet, no cough, no sweats, and no hæmorrhage, although during the past three months he had noticed some oozing from his gums. He was admitted for increased weakness, slight nausea, and loss of appetite. He had lost considerable weight. He knew of no one with a similar trouble.

Such was the history given by the patient. After his death, however, his mother gave the interesting information that during his vacation trip she thought he did not look well, and on one occasion long-continued hæmorrhage followed the extraction of a tooth.

Physical examination.—The patient was rather sallow in color and appeared very weak. He was of fair muscular development, but had evidently lost some weight. The skin was thin and transparent, the superficial veins quite visible; the scleræ were pearly, the conjunctivæ pale and not bile-stained. The eyes were negative.

The mucosæ were very pale; there was a slight hæmorrhage on the inner surface of the lower lip. The tongue was heavily coated.

The tonsils were not visible, there was no obstruction to the nares, no palpable glands in the neck, and none in the axillæ or inguinal regions. There was no evidence of enlarged glands in the abdomen.

The veins of the neck and thorax were full, those on the left side being more so than on the right, and showed a positive, systolic, centrifugal pulse.

The thyroid gland was negative.

The chest was long and flat, and the respiratory movements good and equal on both sides. In the lower left axilla the breath sounds had a tubular modification, with expiration prolonged;

showers of râles on inspiration and a few on expiration. The same was true of the lower back below the spine of the scapula; otherwise the lungs were negative.

The heart was not enlarged; there was a blowing systolic murmur at the pulmonic area, which was heard also at the apex, but not beyond it; otherwise the heart was negative.

The liver dulness began at the upper margin of the sixth rib in the right mammary line, and extended five centimeters below the costal margin. The spleen was not palpable. The abdomen was otherwise negative.

The patient brought with him an excellent blood report made a few days before his admission to this hospital, which read as follows: "Hæmoglobin, 25% (Tallqvist); red corpuscles, 944,000 per cmm.; white corpuscles, 428,000 per cmm.

Differential leucocyte count: Polymorphonuclear neutrophiles, 0.9%; small mononuclears (lymphocytes), 2.0+%; large mononuclears (lymphocytes), 96.0%; eosinophiles, 0.5%; mastzellen, 0.5%.

A few neutrophile and eosinophile myelocytes are encountered. The large mononuclears are unusually large, with nuclei eccentrically placed, and take a very pale stain. Many are egg-shaped and quite rich in chromatin, the latter being scattered over some and collected in bunches in others. Many show degenerative changes, and some are undergoing karyokinesis. Blood platelets are very scarce. Many red cells are microcytic; poikilocytes are absent. Nucleated reds are very scarce, only one megaloblast being found while counting the leucocytes. They take the stain throughout and very few show a ringed appearance." (H. S. H., Asst. Bacteriologist, State Board of Health, Fla.)

On October 31 we found: Hæmoglobin, 17% (Dare); red corpuscles, 752,000; leucocytes, 880,000; large mononuclears, 97.2%; small mononuclears, 1.9%; polymorphonuclear neutrophiles, 0.51%; neutrophile myelocytes, 0.34%; polymorphonuclear eosinophiles, 0.25%; mastzellen, 0.05%.

The predominating cell was a palely-stained mononuclear with vacuolated nucleus, and abundant basophilic protoplasm, whose size varied from that of a lymphocyte to a giant cell. Very few normoblasts were present. It took fully half an hour to allay the hæmorrhage from the pin-prick in the ear, made to get the blood for the above examination.

During the afternoon of October the 31st, the patient grew weaker, and in the evening was unable to sign some business papers.

November 1, at 2.45 a. m., the patient became comatose. His dyspnœa was a remarkably good illustration of air hunger; each inspiration shook his whole body and yet the air passages were perfectly free. He died at 4.30 a. m.

The urine on admission was clear, yellow in color, having a specific gravity of 1012, with acid reaction, no albumin, no sugar, and no sediment. The following day the urine was similar in appearance, over 700 ccs. in amount; its specific gravity was 1013, with acid reaction, no sugar, the faintest trace of albumin, and a few granular casts. There was no acetone, no diacetic acid, and the Diazo test was negative. The temperature varied from 98.9° to 100.2°, and was 100.6° at death; the pulse varied from 112 to 120, and the respirations from 20 to 28 to the minute.

Autopsy, November 1, 1905, 12.30 p. m. No. 2615.

Anatomical Diagnosis.—Acute lymphatic leukæmia; dilatation and fatty degeneration of the heart; hydrothorax left side; œdema of the lungs; subcutaneous, subserous and submucous ecchymoses; chronic gastritis; pyoid hyperplasia of the bone marrow of the vertebræ.

The following is a very brief abstract of the anatomical report:

The body is well built and well nourished. The inguinal, cervical and axillary glands are palpable, firm, but not much enlarged. The abdominal subcutaneous fat is plentiful in amount. Scattered through it are minute cherry-red areas, from 1 to 3 mm. in diameter: similar nodules are in the mesenteric fat. Mesenteric lymph glands are small. The left pleural cavity contains many old fibrous adhesions over the anterior aspect of the lung. In the right pleural cavity are about 5 ccs. of blood-stained, cloudy, serous fluid.

Heart.—There are numerous small hæmorrhages under the epicardium. The cavities contain firm clots, deep red in the dependent parts, and above consisting of layers varying in color from grayish-pink to light yellow with a greenish cast in places.

The lungs are quite free from interesting features.

The spleen measures 14 by 7.5 by 3 cm., and weighs 185 gms. The capsule is slightly thickened at points, but translucent for the most part. On section the trabeculæ are inconspicuous. The pulp is of a pale brownish-red color with small hæmorrhages scattered through it. The Malpighian bodies are enlarged, but are not sharply outlined. The organ is firmer than normal.

The liver weighs 1800 gms., and measures 25 by 19.5 by 9.5 cm. Its edges are sharp and somewhat irregular. The surface and cut surface are uniform in color, with no macroscopic nodules. The gastro-hepatic lymph glands are enlarged and fairly firm, with an opaque, grayish-pink color and a slightly rusty tinge on section.

The stomach, pancreas, kidneys, adrenals, bladder, genital organs, are all without lesions worthy of note here.

The aorta is narrow in its lumen, measuring when opened 5.5 cm. at the arch and 4.2 cm. at the celiac axis. The lymph glands along it are prominent, but not especially enlarged. On section they are rather opaque, of a yellowish-white color, with here and there small areas of congestion.

Intestines.—The mucosa of the jejunum is pale. It appears somewhat thickened as also do the transverse folds. The surface is coated by a considerable amount of mucus. As one approaches the ileum he finds here and there an area of injection and submucous ecchymoses, together with a few small, slightly elevated nodules surrounded by an area of injection; they are slightly elevated, but show depressed pigmented areas giving them the "shaven-beard" appearance. The appendix is normal. The large intestine is also normal save for a few nodules similar to those above mentioned.

The ribs appear to be free from bone-marrow. The trabeculæ of the bone stand out prominently, but have no tissue between them. The bone marrow taken from the center of the femur is fatty, but shows slight hyperplasia at its periphery, the peripheral part here being a little more opaque and of a grayish color. In the vertebræ the marrow is soft, opaque, grayish-pink in color, and almost fluid, resembling somewhat the blood clots in the vein.

Microscopic Examination.—*Blood Clots.*—The nucleated cells predominate, especially those of the large lymphocyte type; nucleated red cells are numerous. Mitotic figures are present.

Bone-marrow.—The femoral bone-marrow is fatty. Between the fat cells are but few cells of the blood group, and these are apparently in vessels. The rib and vertebral marrow resemble the clots in the heart, and the nucleated red cells are few.

Lymph glands.—In the bronchial tubes the lymph cords and follicles are small, and the cells are of the large type. The lymphocytes are few. The mesenteric glands show a chronic lymphadenitis with marked thickening of the fibrous structure, especially of the medulla of the gland.

Spleen.—The fibrous framework of the pulp is increased in amount. The Malpighian corpuscles are very small, showing hyaline masses, some of which are agglutinated red blood cells.

Intestines.—There is chronic enteritis with sclerosis at the base of a Peyer's patch, and areas of necrosis at the center of a patch. There are no lymphoid nodules in any organ.

This is a typical case of acute leukæmia of the so-called

lymphatic or lymphoid, or better still, myeloblastic type. Its duration was about two months, and its most striking features were the very high white cell count and the extreme anæmia.

The case was not only truly myelogenous but the lesion of the bone-marrow was apparently localized in the vertebral column. The spleen, liver, lymph glands, tonsils, and lymphatic deposits along the intestine were all free. The rib and femoral marrow were free from lesion, which may explain the absence of tenderness of the long bones, as was present in the cases of Ritter,[1] Türk,[2] and Gordinier.[3] This case illustrates a point emphasized some time ago by Grawitz and others that marrow from several bones must be examined before any statement can be made concerning their involvement. Had the pathologist stopped in this case with the examination of the ribs and femur the case could have been reported as "acute leukæmia without bone-marrow lesion." In reporting such cases the pathologist should state what marrows were examined. This Drozda[4] did not do, and Dennig[5] may not have looked far enough.

This case was acute, though lasting about two months; not a *leukæmia acutissima* of from four to ten days' duration. It belongs perhaps to the acute cachectic group.

There was hypoplasia of the aorta, its diameter being quite narrowed, which reminds one of chlorosis, a disease which Virchow considered congenital, and associated with hypoplasia of the cardiovascular system. The same may have been true of Pfannkuch's case,[6] who was pale for years, also of the case of Sondern and Mendelson.[7]

The patient's mind, as also in Case II, showed considerable mental hebetude at the last; but earlier in the disease, as is the rule, clearness of intellect and comfortableness of condition marked the two cases.

Acute leukæmia is a condition which may be suspected but cannot be diagnosed without a blood examination. It is protean in form, suggesting both in onset and course many other diseases, among which are acute tonsillitis, diphtheria, scurvy, typhoid fever, malaria, tuberculosis, ulcerative endocarditis, purpura hæmorrhagica, septicæmia, pyemia, pernicious anæmia, and osteomyelitis.

A common form is the "typical" form suggesting chronic leukæmia and differing from it only in its greater acuteness and severity. There is sudden enlargement of the lymph glands of all or of certain groups. In some cases, the glands of the mesentery and the lymphatic tissue along the intestine are involved. The tonsils are enlarged, sometimes they almost touch; the thymus persists.[8] There are even lymphoid nodules of the dura mater.[9] The spleen is usually enlarged, early, if not at first, and the liver also. In these cases the diagnosis is easy since the clinical picture suggests leukæmia, but great difficulties are in the way of the determination of the acuteness of the case, since a preceding, latent, chronic leukæmia is very hard to rule out. One is usually safe in assuming that the blood condition has lasted at least as long as the discovery of enlarged glands or large spleen (but see page 84). To find the spleen large and hard on first examination is evidence against acute leukæmia, hence we have ruled out some cases reported in literature under this title. One may expect to watch the spleen grow in size and firmness. Yet this is not always true. Cattin[10] reports an acute case in which after four weeks' illness the spleen weighed 2500 gms. In some cases the lymph glands enlarge late and then increase rapidly in size.

The acute infectious type is not uncommon. At first it simulates typhoid fever, and later not one element of acute streptococcus septicæmia is absent except the demonstration of the organism. Case II is an excellent illustration of this type. The high fever, continuous or intermittent, the chills and sweats, the extreme prostration, rapidly developing anæmia, even the keen mind suggesting a streptococcus infection, all make a very suggestive picture. There are some (Rose Bradford, Barlow, and Osler) who hold that these cases are acute infections in which the changes in the blood are but a blood reaction, and a very different disease from the ordinary chronic leukæmia. It is certain that true septicæmias can produce a blood picture quite like acute leukæmia, and in the bone-marrow of cases otherwise clearly acute leukæmia organisms have been found. Holst[11] reported three such cases of acute leukæmia. In the first streptococci were isolated from the exudate of the knee and at autopsy from the lymph glands and blood. From the second bacilli and streptococci were isolated at autopsy. In the third streptococci were isolated from the bone-marrow. The abstract of this papepr in French gives no details of the cultures. Again, only an infectious disease would be likely to produce both the blood and marrow changes, and acute enteritis, acute pleurisy, acute bronchitis, acute endocarditis, and acute nephritis, all of which were found in our Case II.

It has long been known that acute infections may cause a high leucocytosis with many myelocytes, and resemble acute myelocytic leukæmia, also a blood picture with normal leucocyte count but the formula of acute lymphoid leukæmia. Holst's second case had a count of 8300, 77% of which were large lymphocytes, 14% small lymphocytes, and 8.3% polymorphonuclear neutrophiles. In his third case the count was 8400 and the large mononuclears 93%. The latter was clearly a streptococcus infection of the marrow. Whether all our cases of acute leukæmia will be shown to be due to infections is the question.

[1] Deut. Med. Wchs., 1904, p. 1042.
[2] Ibid., 1903, p. 355, Ver.
[3] Johns Hopkins Hosp. Bull., Oct., 1904.
[4] Deut. Med. Wch., 1902, Vol. 28, p. 340.
[5] Münch. Med. Wchs., 1901, No. 4, p. 140.
[6] Münch. Med. Wchs., 1904, Vol. 51, p. 1732.
[7] N. Y. Med. Jour., 1905, Vol. 82, p. 1154.
[8] Gordon's Case, Lancet, 1906, II, p. 1759; Kelly's Case III, Trans. Assoc. Am. Phys., 1903, XVIII, p. 481; and Phear's, Tr. Royal Med. and Chir. Soc., London, 1901, p. 453
[9] Chloromata (?), Drozda, Wien Med. Wchs. 1903, LIII, p. 405.
[10] Anjou Méd., Angers, 1903, X, p. 325.
[11] Norsk. Mag. f. Lægevidenskaben, 1904, p. 1098.

Schupfer[12] brought evidence against the infectious nature of this disease by injecting blood from such a patient into cancer cases, and since no change occurred in the cancer, which as a rule reacts in a marked degree to acute infections, he considered the infectious nature of acute leukæmia doubtful.

Other cases suggest a local collection of pus, as abscess of the liver (see page 80).

A large group of cases assumes the "hæmorrhagic form." Some suggest purpura hæmorrhagica, or morbus maculosus Werlhofii, as in Osswald's case[13] and Shattuck's case[14] of "infectious purpura." The patients are covered with subcutaneous, submucous, and subserous hæmorrhages; there are hæmorrhages into conjunctivæ, retinæ, and from nose,[15] mouth, stomach, and bowel, and they may die from cerebral hæmorrhage (Gordon). They sometimes develop local hæmatomata, as did Barié and Salmon's patient,[16] in which case a hæmatoma the size of a nut appearing just below the angle of the right scapula, grew so rapidly that on the third day it was the size of an infant's head. It was later opened and 1300 gms. of blood evacuated. These cases are usually fulminant, the anæmia extreme, and the diagnosis made at autopsy.

Another, to which Case I belongs, is the acute cachectic group. Sudden inexplicable weakness, loss of flesh, shortness of breath (Türk, Grawitz, Gordinier), and prostration increasing till death, with perhaps a few petechiæ and ulcers in the mouth, if one looks sharply, yet not so fulminating a course nor with such high temperature as the former, if indeed there is any fever; such is the clinical picture. This is the group mentioned by Josserand as simulating pernicious anæmia. These patients are very pale with a slight but definite jaundice, in addition to the features above mentioned. But the tint is not the same; there is not the brownish pigmentation of primary pernicious anæmia, but rather a whitish pallor, and there is emaciation. They look sicker.

The "bucco-pharyngeal" mode of onset first emphasized by Gilbert is by far the most common, and these symptoms may continue so long that the cases constitute a distinct group, although the majority of cases in the other groups also begin in this way. There are very few cases in which one or more lesions in mouth or larynx cannot be found if carefully looked for. It is even believed that the portal of entry of the disease is through these mouth and throat lesions.

This group is divided into the pseudoscorbutic and the pharyngeal forms. In the pseudoscorbutic type swelling and tenderness of the gums may be the first sign. There is a severe stomatitis often gangrenous, with oozing from the gums, areas of necrosis along the edge of the alveolar processes, and submucous hæmorrhages. With the stomatitis the submaxillary glands are enlarged. Many cases appear to start with the removal of teeth, or at least the hæmorrhage following that operation is the first symptom. Such was true of Case I, of Grawitz's case,[17] from which fourteen teeth were extracted. Some cases resemble malignant disease of the upper jaw (Bradford). Gangrenous ulcers of the mouth are very common, especially ulcers connected with decaying teeth. These may precede the blood changes, and are the symptoms from which the disease dates. The cases of the pharyngeal group begin usually as an acute follicular tonsillitis or as diphtheria as did Edsall's,[18] Patoir and Dehon's[19] and Surmount's.[20] So common are such cases that it may be stated as a dictum "with diphtheritic throat and purpuric eruption in a child, look at the blood," (Jeanselme and Weil.[21]) The blood condition has been attributed to the use of anti-diphtheritic serum. Such cases are probably acute leukæmia beginning with a gangrenous pseudoangina. The most common sequence in children is, "diphtheria" with gangrenous tonsils, then "purpura hæmorrhagica," then enlargement of lymph glands, liver, and spleen, then "lymphatic leukæmia." In other cases, especially in adults, the sequence is, severe anæmia with intense pallor and extreme feebleness, then profuse hæmorrhages from nose, mouth, etc., then the purpura, and from the first a gradual enlargement of the lymph glands, liver, and spleen. In Lazarus's case[22] the tonsils were covered by a purulent exudate containing staphylococci and streptococci. It is interesting that the cervical glands may become enlarged before the tonsillar signs appear, evidence against the primary nature of the latter lesion. Sometimes a hæmorrhage into the tonsil is the first sign. Gangrenous ulcers in the tonsil have been mistaken for luetic chancres. Adenoids are sometimes abundant in the posterior nares.

In addition to the purpuric cases is a group in which cutaneous lesions are the most striking features. It is possible that Mannaberg's case[23] was one simulating lues rather than a maculo-papular syphilide which later became leukæmia. Holst[24] reports a case with thickly studded, painless nodosites on the skin of the face, breast, and back, some even the size of a pea. Stevens' case[25] is interesting since he thinks that the subcutaneous lymphocytic nodules which varied in size from a millet seed to a threepence in size, were chloromata. A discussion of the skin lesions is given by Aguinet and Ribadeau-Dumas.[26] Masses just above the elbows appeared in our Case II, evidently of lymphatic tissue, which we feared would become gangrenous.

Some cases begin as an acute gastro-intestinal intoxication,

[12] Reviewed in Jour. Am. Med. Asso., 1905, II, p. 882.
[13] Corresp. Bl. d. Schw. Aerzte, 1904, Vol. 34, p. 145.
[14] Jour. of Cut. Dis., 1904, II, p. 118.
[15] Elder and Fowler, Edinb. Med. Jour., 1904, Vol. XVI, p. 502; and Blackader, Arch. of Ped., 1905, Vol. XXII, p. 890.
[16] Bull. et Mém. de Soc. méd. de Paris, 1903, XX, p. 193.
[17] Klin. Path. des Blutes, 1902.
[18] Am. Jour. Med. Sc., 1905, Vol. 130, p. 589.
[19] Echo méd. du Nord, Lille, 1905, Vol. IX, p. 301.
[20] Ibid., 1904, Vol. VIII, p. 553.
[21] Pédiat. prat., 1904, II, p. 52, Bull. et mém. Soc. méd. des Hôp. de Paris, 1904, XXI, p. 185.
[22] Deut. Med. Wchs., 1905, Vol. XLII, p. 1209.
[23] Deut. Med. Wchs., 1902, Vol. 28, Ver. p. 70.
[24] Norsk. mag. f. Lægevidenskaben, 1904, p. 1098.
[25] Glasgow Med. Jour., 1903, Vol. LX, p. 1.
[26] Arch. gén. de Méd., 1905, II, p. 1928.

with severe vomiting and diarrhœa.[27] Diarrhœa is a very common symptom (Case II). Some begin as acute nephritis with œdema of the feet and of the eyelids so marked that the patients can hardly see. Türk's case had albumosuria.

The number of cases with pulmonary features is so great that an intimate relation between the conditions may be suspected. Some begin as an acute bronchitis,[28] even a bloody bronchitis. Others have acute pleurisy, Case II. The lymphomatous infiltrations with secondary necrosis and ulceration in the mucosa of larynx and pharynx were well described by Virchow. The same occur in the bronchi. Other patients have pain in the joints. Pain over the long bones is a common feature (see page 84). Two cases have recently been reported as associated with pregnancy.[29]

Cases with various pareses are reported, as of the external rectus of the eye, of the leg muscles, etc.

The *blood* in this case was typical of acute leukæmia; the severe anæmia, only 752,000 red cells, the high leucocyte count of 880,000, exceeding the red count, the few signs of regeneration, the large percentage of large lymphocytes, 97.2%, and the great scarcity of granular cells.

Although the red cell counts in this variety are usually very low (very rarely any lower than this case[30]) a progressive severe anæmia is almost an essential symptom, yet this is not always true, as in our Case II; Kelly's Case III with reds 3,590,000; Larrabee's[31] with reds 4,392,000; Wister and Gwyn;[32] Shattuck[33] with 3,024,000; Gordon;[34] and Türk's with 6,976,000 (Hb. 17.2 gms.).

In some cases the red count rises, due perhaps to diarrhœa, etc., as in our Case II, and Rosenberger's.[35] In all cases rapid destruction of red cells does not occur, although it is the rule. The relation of these cases to "pernicious anæmia" since many believe that both are the result of buccal infections, as well as to acute leukæmia, chloroma,[36] and sarcomatosis leukæmia,[37] multiple myeloma with the presence of Bence Jones' body in the urine, and lymphosarcomatosis[38] is an interesting problem.

The color index in Case I, was over 1, *i. e.*, 1.2, a point which McCrae[39] has emphasized as a very common feature of the acute cases.

The failure of the blood clots to contract, so much emphasized by Hayem and his school,[40] has not been much studied here.

The leucocytes in this case numbered 880,000, rather high for this form in which the counts are more apt to run from 150,000 to 200,000 cells. It is unusual for the whites to outnumber the reds as in this case their ratio being 1.2 : 1. The highest count in the three cases reviewed by Hamman[41] was 958,000. These were all "lymphatic" cases, but in Pfannkuch's case[42] of myelocytic leukæmia, they numbered 1,000,000. Slade's case[43] had a count of 1,300,000 but it was not an acute case, although often quoted as such. One feature quite marked in our Case II and often seen in acute leukæmia, judging from the literature, is the rising count. It is almost normal at first when the symptoms are severe enough to bring the patient to the clinic; it then increases till its height may lead one to suspect the diagnosis, and reaches a fairly high point at death.

In Case I the cells rose from 12,400 to 184,000 in thirteen days, a rise of 13,200 cells per day. A low count on admission rising rapidly later was also a feature of Kelly's case (17,000, 35,000, 105,400, 119,500, 163,000, counts almost the same as ours). In McCulloch's case[44] the cells rose from 15,000 to 37,600, and in Bensaude's case[45] from 44,640 to 135,780 in eight days. In Januszkiewicz's case they rose from 52,500 to 165,000. These very rapid variations in the count are explained as evidence of the rupture of "sarcoma" cells through the walls of the blood-vessels.

In still other cases the count after rising falls before death, as in Nichols' case,[46] in which the counts were 67,800, 134,800, 29,600, and 22,150. The first of Holst's three cases,[47] and one from which organisms were isolated, is most instructive. The counts of this case of clear acute lypmhoid leukæmia were 93,000, 130,000, 58,000, and one day before death, 1600. This drop may be due to the production of many very sensitive cells or to "exhaustion" of the bone-marrow. Wolff[48] mentions cases of leukæmia which became "pseudo-leukæmia." He considers a drop in count a bad sign if due to aplasia of the hæmatopoietic organs. It is also his opinion that many periods of apparent improvement with low count are really pseudoremissions due to lytic processes in very sensitive cells (see page 76).

The cells of Case I were chiefly mononuclear nongranulars, 97.2% large, 1.9% small. Other cases may exceed this by a small fraction of this last per cent, as Fatal's of 99.8%.

Acute leukæmia with normal blood count but with characteristic formula is not a rare clinical occurrence, and the opinions concerning it vary (see page 83).

[27] Pfannkuch, Münch. Med. Wchs., 1904, Vol. LI, p. 1732.
[28] Gordinier, loc. cit., Our Case II.
[29] Lazarus Deut. Med. Wchs., 1905, Vol. XLII, p. 1209.
[30] Laurent's case, Lyon Méd., 1906, p. 892, had a count of 750,000 cells.
[31] Bost. M. and S. Jour., 1905, Vol. 152, p. 40.
[32] Univ. of Penn. Med. Bull., 1904-5, XVII, p. 42.
[33] Loc. cit.
[34] Lancet, 1906, II, p. 1759.
[35] Am. J. Med. Soc., 1904, Vol. 128, p. 583.
[36] Bramwell, Trans. Edinb. Med. Chir. Soc, 1902, Vol. 21.
[37] Drozda, loc. cit.
[38] Türk, Wien. Klin. Wch., 1903, XVI, p. 866.
[39] Brit. Med. J., 1905, I, p. 404.
[40] Bull. et mém. de Soc. méd. d. hôp. de Paris, 1903, XX, p. 167.
[41] Am. Med., 1904, Vol. VII, p. 139.
[42] Loc. cit.
[43] Lancet, 1905, I, p. 572.
[44] Montr, M. J., 1904, Vol. XXXIII, p. 580.
[45] Bull. Med. Par., 1904, XVIII, 1101.
[46] Am. Med., 1903, Vol. V, p. 827.
[47] Loc. cit.
[48] Deut. Med. Wchs., 1905, Vol. XXXI, p. 85.

Since Neumann's work it has been a more and more generally accepted idea that of the leukæmias the acute at least are purely myelogenous. This being granted it may possibly be better to drop the time-honored terms, "myelogenous" and "lymphatic," (Ehrlich) for "lymphoid" and "myeloid" (Pinkus), or "lymphocytic" and "myelocytic," or better still, "myeloblastic" and "myelocytic" (Weber). There are two cells of importance, present in large numbers, and according to the presence of these the case is named. If the large non-granular mononuclear resemble a much enlarged lymphocyte it is lymphatic, lymphoid, lymphocytic, or, believing these to be the most primitive marrow cells, myeloblastic. If the granular mononuclear is the one increased, myelocytic. Concerning the latter cells most authorities are agreed. These large non-granular mononuclears have received a variety of names; large lymphocyte, non-granular myelocyte, lymphoid cell of marrow, myelocytoblast, myeloblast, premyelocyte, myelogonien, and undifferentiated leucoblast. We believe the sooner the term lymphocyte, and the compromise terms ending in "oid," are dropped, the better. These cells are round or oval in shape, with a relatively large nucleaus, round, oval, notched, or "bean"-shaped, poor in chromatin yet often with a good network, and a rather scanty protoplasm, more basophilic than the nucleus. The nucleus is often eccentric. They were first described by Fränkel in 1895 as characteristic of acute leukæmias. In this he was wrong, as others soon showed. They occur in all leukæmias. Somewhat similar cells are numerous in typhoid fever and malaria and perhaps are a constituent of normal blood if one takes the trouble to look for them. They are very fragile. They occur especially in acute leukæmia in large numbers. Januszkiewicz[49] says that no case of acute leukæmia is reported in which they did not predominate. It is possible that the cases with few present were only acute exacerbations of a chronic leukæmia, or that these cells were destroyed in the technic. Every transition from these to granular myelocytes occurs and the line drawn is only arbitrary. It may be that they are only an early generation of cell which later changes to one of the various granular cells, or perhaps to a red cell. It may be that in the myelocytic cases the descendants of these same cells which have changed to granular cells are increased; perhaps the disease attacks a different generation of bone-marrow cell. In favor of this idea is the greater anæmia which accompanies the former type (in this case only 750,000 reds) the absence of nucleated reds and other signs of regeneration. It is possible that the relative proportion of these cells is an index of the severity or rather profundity of the bone-marrow involvement, the myeloblasts predominating when the marrow lesion strikes at the root of the cell genesis, the myelocytes when the involvement is less fundamental. Of course the question of severity and duration of disease may not depend on the bone-marrow lesion alone. If this is true then some cases might change from myelocytic to myeloblastic as the disease progresses, and this seems to have occurred in Wilkinson's case,[50] and in v. d. Wey's.[51] Ehrlich, among his first papers on the blood, mentions a case in which toward the end non-granular cells seemed to replace the granulars "as if the ability to form neutrophile material was lost." Weber[52] reported a case "remarkable amongst cases of acute leukæmia on account of the great numbers of myelocyte-like cells present in the blood-forming organs, yet the greater proportion of colorless cells both in the blood and in the tissues belong to the lymphocyte type." He refers to acute lymphoid leukæmia as the most "primitive" type of leukæmia and the splenomedullary as the "most highly differentiated" of all. He gives a scheme of the leukæmias. Browning[53] considers the possibility that acute lymphoid leukæmia is the result of a reversion to the fœtal bone-marrow. He mentions the relative infrequency of myelocytic leukæmia in children. Fowler[54] reported the youngest, a child of five years of the acute "mixed" form.

But the line between the non-granular large lymphocyte and granular myelocytes is only arbitrary, depending on technic and on opinion. The former, even in the most beautiful specimen, may show none or all stages of granulation.

We have no intention of going into this question further. The discussions of these cells and this disease, whether always myelogenous or not, is found in Reed[55] and Kelly.[56]

The most interesting point to us is the demonstration of the fragility of so many leucocytes. The study of fresh blood and the use of the various methylene-blue eosin stains with methyl alcohol as fixative have taught us much concerning the large mononuclear cells, which are often as large as giant cells, and are found in all normal blood, but especially in typhoid fever and malaria. Grawitz has called attention to the fragility of these cells in the bone-marrow, considering that the "younger" the cell the more easily is it destroyed. Using Ehrlich's stain only unrecognizable blotches remain of these cells, as well as of the large macrophages of typhoid fever and malaria which are easily studied in the fresh specimens. Wolff states that using Romanowski's stains the large mononuclears are 10% instead of 2 to 4% as with Ehrlich's stain. Years ago Uskow emphasized the fact that in our ordinary leucocyte counts we lost some cells which go to pieces in the dilute acetic acid. We have given some attention to this point in normal bloods, but have found that the count with Toisson's is usually lower than with acetic, due we believe to the low dilution of the blood; since we try in a 1:200 dilution, in which the reds are preserved, to judge of 8000 leucocytes, counting 8 millimeter squares each averaging 4 cells, this means that the chance for error is enormous as the multiplier is so large; and the count will average lower, using Tois-

[49] Loc. cit.

[50] Lancet, 1903, I, p. 1739,

[51] Deut. Med. Wchs., 1896, p. 287.

[52] Trans. of the Path. Soc. of London, 1903, Vol. LIV, p. 286.

[53] Lancet, 1905, II, p. 507.

[54] Internatl. Clinics, 1903, Vol. III, p. 217.

[55] Am. Jour. Med. Soc., Oct., 1902.

[56] Trans. Assoc. Am. Phys., 1903, XVIII, p. 481.

son's fluid, since the danger is of overlooking lymphocytes, than in a smaller count made with acetic acid, where lymphocytes are counted and but a few large mononuclears dissolved. But this case offered us a good opportunity to put the point to the test; hence the writer made careful leucocyte counts from drops of blood taken at the same time, using in one case dilute acetic acid, in the other Toisson's fluid. The counts were as follows; using dilute acetic 677,000 per cmm.; using Toisson's fluid, 880,000. Hence 203,000 leucocytes per cubic millimeter must have disappeared in the acetic acid mixture. Since the "large lymphocytes" were so greatly in the majority it is fair to suppose that these cells disappeared. Wolff believes (but gives no case to illustrate the point), that this destruction of cells may be so great as to explain apparent remissions in an attack when actually there was a high count of these cells. A few years ago we attempted to settle this question from a different point of view in a case of chronic myelogenous leukæmia with ascites. Our endeavor was to "grow" these cells artificially so as to watch their development. While the ascitic fluid was being drawn off, blood counting pipettes were filled exactly as if for a blood count at a dilution of 1:200, taking the blood from the ear, and instead of acetic acid using the ascitic fluid as diluent. Six pipettes were thus filled under as sterile conditions as possible, sealed and placed in a thermostat at blood temperature. On successive days the pipettes were well shaken and the blood cells counted, then the tubes resealed. Smears were also made, stained, and studied, with a view to determining which cells disappeared first. This test was not satisfactorily finished owing to the press of other work, but we were sure the cells to remain longest were the "fragile" red cells, especially the nucleated reds and these were grouped as if they had multiplied. Other small mononuclears were abundant, some polymorphonuclears, but what pleased us especially was to find some large mononuclear neutrophiles well preserved, showing that these cells at least are not so fragile as might be supposed. Nevertheless it is not at all strange that a fluid which will lake easily all non-nucleated red cells should be destructive to these young leucocytes with large vesicular nucleus containing little chromatin and so very sensitive to other reagents.

CASE II.—*A case of acute (myelogenous?) leukæmia, resembling a septicæmia, with leucocytes almost all achromatophilic.*

R. B., age 27 years; male; white, watchman; Gen. No. 55,828. Admitted Aug. 3, 1906. Died Aug. 16, 1906. Clinical diagnosis: Acute mixed leukæmia with typhoidal course.

The patient complained of "fever."

His family history was negative.

The past history was uneventful; he had always enjoyed good health. As a child he had measles, mumps, and whooping cough, but he never has had scarlet fever, diphtheria, pneumonia, rheumatism, chorea, tonsillitis, or malaria. He had no symptoms pertaining to the eyes, ears, nose, or throat. He denied headache, dizziness, or any nervous trouble before the present illness. Five years ago he had a cough of eight months' duration, with slight expectoration, though not bloody, without night sweats, and which did not influence his general health. He denied any gastrointestinal symptoms, such as nausea, vomiting, abdominal pain, diarrhœa, bloody stools, mucus in stools, etc. His appetite had always been excellent, and his digestion good.

His genito-urinary history has been negative, without venereal infection, and with no pain or frequency of micturition. He denied any skin eruption at any time.

His habits have always been good, and, so far as alcohol is concerned, he drank only an occasional glass of beer or whisky. His average weight was 187 pounds.

Present illness.—The patient stated emphatically that his present illness began acutely eleven days ago, with general malaise and pain in the limbs. On the next day the pain in the limbs was worse, he had no appetite, and yet he worked. On the fourth day he gave up work, feeling very sick, with griping pains just above the navel. He felt still worse on the fifth day and his physician gave him a purge, since which time he has had ten or more movements a day, none of them bloody. He has had no chills, or chilly feelings, but he has sweat profusely. He had no nose-bleed, no cough, no nausea, no vomiting, and no headache until admission.

Such is the story as told by the patient and by his wife. Just before his death, however, on questioning her more closely, we learned that during the past year the patient had frequently complained of headache, "weak spells," and "fever," and hence was frequently off duty.

Physical examination, August 4, 1906.—(The following notes are very much condensed from the original reports). The patient lay comfortably in the dorsal decubitus. His expression was bright and animated; there was no pain. The tongue was quite clean. The pupils reacted actively to light and accommodation, the external muscles balanced well. The pulse was 84 to the minute, and was not dicrotic.

Lungs.—The right lung was clear on auscultation and percussion in front and in axilla. Over the left front there was slightly diminished resonance, distant breath sounds, and many fine crackling and sibilant râles. Over both backs the percussion note was about equal, the breath sounds were distant, and the râles similar to those in left front.

Heart.—The point of maximum impulse was in the fifth interspace just inside the nipple line. There was a soft systolic blow over the body of the heart, but no accentuation of the pulmonic second sound.

Abdomen.—The abdomen was rather distended; it was symmetrical. Areas of pigmentation caused by two mustard plasters covered the epigastric angle and the umbilical region. The liver dulness began at the upper border of the sixth rib in the right mammary line, and extended to the costal margin. The spleen could be felt, but palpation was very difficult. The area of splenic dulness was not increased. There was dulness in both flanks. The patient perspired profusely; the profuse sweat had a very sour odor. There were no rose spots. The shins were clear, and there was no œdema of the ankles.

Blood examination.—Red cells, 4,300,000; leucocytes, 12,000; blood pressure, 95 mm. Hg. (systolic).

The temperature on admission last evening was 104°: to-day it fell to 101° and then rose again to 104°. The pulse has varied from 80 to 104, and the respirations from 20 to 28. The patient passed but one fluid stool and 370 ccs. of urine. The Diazo test was negative, and the Widal test was negative. On this day we doubted the diagnosis of typhoid fever with which he was admitted, and suspected septicæmia of some sort. The blood cultures made to-day remained sterile.

August 5.—At 3.30 a. m. to-day the patient complained of griping "cramp-like" pains just above the navel, each pain being of moderate severity, lasting about one minute and recurring every 10 or 15 minutes. Each pain was accompanied by the desire to defecate. His expression was now (5.30 a. m.) free from anxiety; he was sweating profusely. There was no change in tempera-

ture or pulse, no nausea, no vomiting, and no pain on micturition or on defecation. The abdomen was full, its movements on respiration good. There was slight rigidity and some tenderness on the right side, as also some tenderness above the umbilicus, but no muscle spasm. Leucocytes, 12,400. These pains recurred at intervals during this day. The bowels moved four times; the stools were negative. He was nauseated at 6.30 p. m. and several times later, but did not vomit. The abdomen became (7.30 p. m.) slightly fuller than in the morning, but its respiratory movements were good. On the right side of the abdomen there was slight muscle rigidity, especially in the iliac fossa, but no muscle spasm, and little pain on deep pressure, except just above the umbilicus where pressure also caused the desire to defecate. There was no pain on defecation or urination. The liver dulness was the same as before: the dulness in the flanks was distinctly shifting when the patient rolled on his side. The sibilant râles were now universal throughout the lungs. At the fifth right interspace in front and at the base of the right axilla, the percussion note was impaired, the breath sounds were distant, yet not tubular, and the râles were quite numerous. The pulse varied from 80 to 104 and was very dicrotic; the respirations, from 20 to 28, and the temperature, from 101° to 104°. There had been six fluid stools and he had voided 1100 ccs. of urine. Cultures made to-day from the urine remained sterile. Leucocytes, 21,000; no malaria parasites found. We now asked ourselves if it might not indeed be typhoid fever admitted with some abdominal complication.

August 6.—On this day a few petechiæ were found over the manubrium, otherwise the signs were unchanged. The temperature ranged from 102.6° to 103.9°; the pulse, from 84 to 120 and was dicrotic; the respirations, from 20 to 32. He passed five stools, and 2220 ccs. of urine. Leucocytes, 21,800. The Widal test on this day was again negative.

August 7.—On this day the patient was much nauseated and vomited repeatedly. The edge of the liver was much more easily palpable and more tender on pressure, especially at the gall bladder region, suggesting a cholecystitis. The rectal examination was negative. The temperature ranged from 102.5° to 104.1°; pulse, from 96 to 120; respirations, from 24 to 28. There were to-day three stools and 2590 ccs. of urine. The number of leucocytes was 33,000.

August 8.—To-day the spleen measured 4 cm. below the costal margin, and the liver, 1.7 cm. A definite friction rub was heard at the base of the right axilla. The temperature varied from 102° to 103.1°; the pulse from 96 to 120; the respirations from 24 to 28. He voided 3390 ccs. of urine, and had two stools. The Widal test was negative for the third time. Leucocytes, 56,000. The increase in size of the liver, the tenderness along its edge the friction rub over its lateral surface, together with the other signs of a pyæmic process, suggested liver abscess so strongly that we obtained his consent to an exploratory operation. But at just this point attention was attracted to the blood picture. Hasty examination had suggested a polymorphonuclear leucocytosis, but now we began to try to make an accurate differential count. Leucocyte count, 56,000.

August 9.—The nausea still continued. To-day there were found at each elbow an infiltrated area which suggested a chain of large lymph glands, but was probably a diffuse lymphocytic infiltration. The other lymph glands were not enlarged. There was a fresh crop of purpura in the lower left axilla. The temperature varied from 100.6° to 103.1°; the pulse, from 100 to 120; and the respirations, from 20 to 32. There were to-day six stools, and 3080 ccs. of urine. The ward physician to-day reported that he had used up a whole box of cover slips trying to get a well-stained blood specimen and had failed. The nearest that could be ascertained was: Polymorphonuclear cells, 41%; large mononuclears (granular and non-granular), 44%; small mononuclears, 10%. This statement at once suggested the diagnosis of acute leukæmia, which an examination of the fresh and poorly stained specimens confirmed. The subcutaneous injections of arsenic were begun at once. Leucocyte count, 64,800.

August 10.—The patient to-day expectorated one ounce of bright blood. There was now definite jaundice. A fresh crop of fine petechiæ had appeared over the trunk. The hypodermic punctures were surrounded by a wide area of hæmorrhage. One submucous hæmorrhage was found inside the mouth on the cheek. A coarse friction was now heard also in the left axilla. The temperature had ranged from 101.6° to 103.6°; the pulse, from 90 to 110; and the respirations, from 20 to 32. There had been five stools, and he had voided 4950 ccs. of urine.

Blood examination.—Red blood cells, 4,464,000; hæmoglobin, 88%; leucocytes, 86,000.

August 11.—The patient was drowsy and complained of pain in the lower abdomen and back. There was a necrotic area of the gum at the base of the lower central incisor teeth. There was a loud, leathery-friction rub in both axillæ and in the backs as high as the angles of the scapulæ. Sonorous râles were heard throughout both chests. Otherwise the signs were the same. The temperature ranged from 101.1° to 103°; the pulse, from 100 to 124; and the respirations, from 24 to 36. He had one stool and passed 2060 ccs. of urine. The leucocytes were now 83,100.

August 12.—The general condition remained much the same, but at times, when left alone, he was irrational; at other times, when aroused, his mind was clear. The pulse was of small volume and low tension, 100 to 124 a minute; the temperature ranged from 100.6° to 102.6°: the respirations, from 32 to 44. The diffuse bronchitis and extensive pleurisy persisted. The heart sounds were clear. The petechial eruption in the back was fading. The leucocytes were now 122,000.

August 13.—The condition continued about the same. The temperature ranged from 100.6° to 102.4°; the pulse, from 100 to 124; the respirations, from 30 to 40. He had 11 stools, and passed 1630 ccs. of urine. The leucocytes were 123,000.

August 14.—The patient seemed weaker. The temperature varied from 101.4° to 103.1°; the pulse, from 88 to 120; and the respirations, from 30 to 44. The patient had 11 stools, and voided 1815 ccs. of urine. The leucocytes were 168,000.

August 15.—There was this day some cyanosis, and some dyspnœa. A scattered crop of small purpuric spots had appeared on the face, neck, arms, and back. The heart sounds were much weaker; there was embryocardia. The shifting dulness in the flanks had increased; there was some œdema of the ankles. The temperature ranged from 100.6° to 102.1°; the pulse, from 100 to 120; the respirations, from 28 to 48. He had four stools and passed 1490 ccs. of urine.

Blood examination.—Red cells, 4,600,000; hæmoglobin, 95%; leucocytes, 147,000.

August 16.—The pulse was dicrotic. The jaundice had become deeper. There was some oozing of blood from the mouth. New petechiæ appeared on the forehead, arms, and axillæ. The bronchial râles persisted, the pleural friction was very loud, and there was a louder pleuropericardial rub at the apex of the heart. The œdema of the legs increased. The patient was at times restless, at times irrational, and at times mentally clear. At 9 p. m. to-day he died suddenly. The temperature rose from 101° to 104.4° at death; the pulse varied from 96 to 144; the respirations, from 36 to 40. The bowels had moved five times, and 1220 ccs. of urine were passed before death. The leucocytes this morning were 184,000.

Autopsy, August 17, 1906, 10 a. m. No. 2757.

Anatomical Diagnosis.—Acute ulcerative enteritis and colitis; perforation of ulcer; localized peritonitis; acute suppurative bronchitis and bronchopneumonia; acute hæmorrhagic pleuritis; acute mitral endocarditis; splenic tumor; subserous hæmor-

rhages; acute nephritis; general anæmia; pyoid bone marrow. (The following report is much condensed from the anatomical records.)

The body was well nourished. There was some post-mortem settling of blood to the dependent parts. There were numerous minute subserous hæmorrhages over the intestines, mesentery and parietal peritoneum. The hepatic flexure of the colon was kinked upon itself; the coils were adherent by recent organized exudate. On attempting to separate these coils one opened into the bowels through the thin floor of an ulcer.

The left pleural cavity contained a slight excess of fluid, and the pleura of the left lung was covered by an acute hæmorrhagic and fibrinous exudate. There was a similar exudate over the posterior portion of the right lung. The pericardial cavity appeared to be normal except for a few small hæmorrhages on the surface of the heart.

The heart weighed 300 gms., the right side being much dilated by soft post-mortem clots, which were light brownish-red in color, but without a greenish tinge. The valves were normal except on the mitral flaps at the line of closure there were numerous small translucent nodules, the largest of which stands 3 mm. above the surface of the valve. . . . . The heart muscle was pale, opaque, and rather soft.

Lungs.—These presented numerous hæmorrhages under the fibrinous exudate above mentioned, which were most marked at the posterior portion of the left lower lobe. This lobe on section was deeper in color (than the upper), was moist, and contained numerous areas of hæmorrhage and numerous projecting miliary nodules, which were airless and on pressure yielded a small drop of pus. The bronchi contained purulent material. Otherwise, the lungs were normal (save for the pleurisy above noted).

The spleen weighed 360 gms. and measured 16 by 10.5 by 5 cm. It was adherent to the diaphragm by a fairly fresh fibrinous exudate, and was mottled in appearance with areas of purplish-red and brownish-red. On section the organ was mottled. The trabeculæ was obscured by the increased pulp. The pulp was of a light reddish-brown color with numerous smaller dark red areas running through it. The Malpighian corpuscles were not sharply marked off from the pulp, but they were enlarged. The organ was considerably softer than normal. In it was a firm wedge-shaped, grayish-white infarct.

The liver weighed 2050 gms. and measured 29 by 20 by 8.5 cm. Its surface was uniformly smooth and pale, and its edge rounded. Otherwise, it was negative.

The stomach, pancreas, bladder, genital organs, and aorta all were negative.

The kidneys were similar in appearance. The left one weighed 200 gms. and measured 14 by 5 by 5 cm. The capsule stripped off easily, leaving a mottled surface with some injection of the vessels, and numerous minute hæmorrhages. On section the cortex measured 1 cm. in width, and was somewhat opaque, the striation being regular and sprinkled with numerous small hæmorrhages.

The tonsils were somewhat enlarged, but were otherwise negative.

Intestines.—Throughout the length of the large intestine were numerous ulcers. In the cæcum they were more or less rounded They had fairly undermined edges with clean base, often on the muscularis. There were several in the cæcum which measured 6 to 15 mm. in diameter. The solitary follicles appeared also enlarged and showed small central ulcerations. As one reached the transverse colon the ulcers appeared very ragged. They extended transversely, but chiefly longitudinally, with well defined borders. The floors were fairly clean, but contained a small amount of blackish, necrotic material. This ulceration extended as far as the rectum. In the lower end of the ileum were numerous similar ulcers giving it a worm-eaten appearance. As one passed up the ileum these diminished in numbers till they were shallow and about 5 cm. in diameter. In the lower ileum they seemed confined to the Peyer's patches, but there was no indication of a preceding hyperplasia of the follicles. There were no signs of miliary tubercles on the floor of any ulcer. The mesenteric lymph glands were swollen and had on section a uniform grayish-pink appearance. There was in them no sign of necrosis or caseation.

The bone-marrow of the femur was soft, and of a reddish-gray color, while that of the vertebræ and ribs was similar, but had a more marked reddish-gray, almost pyoid, appearance.

Microscopic notes.—In the lungs were areas of hæmorrhage and areas in which the alveoli were filled with polymorphonuclear leucocytes and some fibrin.

In the liver lobules the cells at the center showed some atrophy. The portal spaces were infiltrated with cells chiefly of the large mononuclear type, but some were polymorphonuclears.

The spleen was extremely cellular. The pulp was infiltrated with cells chiefly of the large mononuclear type. The Malpighian corpuscles were small and quite distinct from the cellular pulp.

The lymph glands showed some hyperplasia, the germinative centers being prominent.

Kidney.—The epithelial cells of the convoluted tubules were swollen, very granular and almost filled the lumen. Some tubules showed the presence of red cells about the glomeruli and larger vessels. There were accumulations of cells similar to those in the portal spaces of the liver. There appeared to be no marked increase in connective tissue.

The bone-marrow of the femur was chiefly fatty, except that in the periphery and about the larger vessels there were accumulations of cells chiefly mononuclear in type, although polymorphonuclear cells were quite numerous. Some mitotic figures were found among these cells.

Dr. Whipple, after studying this marrow in carefully prepared sections, made the following note: "It is a moderately cellular marrow, in which, however, a large percentage of the fat remains. The predominant cells are indifferent cells, there are very few eosinophile cells and giant cells, and only a fair number of nucleated reds. The most unusual feature is the proliferation of fibroblastic tissue in the immediate neighborhood of the small blood vessels."

Intestines.—In the small intestine the Peyer's patches were hyperplastic and showed an ulcerated surface, as well as hæmorrhages into the deeper parts of the patches. The cells were largely of a lymphocyte type, although cells of a larger type were present in considerable numbers, while the polymorphonuclears were fewer. Very few phagocytes or lymphocytes were found.

All the vessels of the various organs showed an unusual number of nucleated cells, especially of the large mononuclear type.

This, then, was a case of continuous fever, admitted on the eleventh and with death on the twenty-fourth day of the disease. That the fever was a continuous one may be judged from the fact that he was given ice sponges every third hour, if the temperature was 102.5° or over, and, although fifty of these were given during the fourteen days, yet not once did the temperature fall below 100.5°.

Among other general features were the absence of any mental symptoms until the very last, and then he was only slightly irrational and but for short periods. Until the last day he was at no time dull and stupid, that is, typhoidal, but always bright and clear-minded. He was without pain if we exclude the abdominal cramps early in the disease. He sweat profusely much of the time, a very sour-smelling sweat,

yet unaccompanied by chilly feelings or fluctuation of temperature.

On admission the diagnosis of typhoid fever was tentatively made awaiting the results of blood culture and the Widal test, which were repeatedly negative. Very soon a septic condition was suspected; the negative Widal test, high temperature, rapid pulse, profuse sweats, leucocytosis, clear intellect so common in streptococcus septicæmia, all suggesting this. But what infection? through what protal of entry? Miliary tuberculosis and malignant endocarditis were discussed. On the eleventh and twelfth days the cramp-like pains in the upper abdomen, which had begun on the fourth day, hence before admission, made us very anxious, fearing that the condition might be after all typhoid infection with intestinal perforation. But these pains and the physical signs accompanying them were never indications clear enough for exploration. Yet, as autopsy showed, intestinal perforation really did occur. There was a perforation of the bowel and local peritonitis, which condition resembled a perforated typhoid ulcer so closely that it required microscopic examination of the tissue to decide the question.

On the 15th, 16th, and 17th days the symptoms-complex was that suggesting abscess of the liver. To the general features of septicæmia and diarrhœa were added an enlargement of the liver, pain on pressure over its margin, and then the appearance of a diaphragmatic pleural friction rub over its lateral surface. We then gained his consent to operation and would have proceeded had the blood condition not been discovered on that day. This case was more suggestive of liver abscess than was that of Sondern and Mendelson;[57] their case had colicky pains suggesting gall-stone colic radiating from the epigastrium, and tenderness at the hepatic notch: pains not unlike those of our case. Unfortunately no autopsy was obtained in their case. In our case as in Sondern's the pains antedated the hospital admission, but by three weeks rather than one. Kelly[58] reports a case of acute lymphatic leukæmia actually admitted to the hospital for operation for abscess of the liver. This patient had the general septic features, and a large tender liver. The ileum showed large infiltrated ulcerated necrotic Peyer's patches resembling typhoid ulcers. He suggested that even autopsy might not always clear up the diagnosis, for typhoid fever may be the anatomical as well as the clinical diagnosis, and in our case typhoid fever was the anatomical diagnosis before the sections were studied microscopically. Thompson and Ewing's case[59] was admitted with abdominal pain, nausea and vomiting. Gordon's[60] had a tender liver, and Gordinier's case suggested a local abdominal trouble. We thought of gastric or duodenal ulcer, but not seriously, although the pain might have suggested it, and the septic features did indicate a perforation. Had he had bloody stools this diagnosis might have been considered seriously, which happened in the case reported by Elder and Fowler[61] where bloody stools alone were the basis of that diagnosis. Stevens' case[62] resembled this case clinically since he also excluded typhoid fever, tuberculosis, malignant endocarditis, and then a septicæmia. His case had the same duration, three weeks, and in both the enlargement of spleen and lymph glands began on about the thirteenth day. They differ in that his had resistent, painful priapism, and the lymph glands increased rapidly in size. Januszkiewicz[63] reported a case which anatomically was in several respects similar to ours, with enlargement of the solitary follicles of the intestines and of the Peyer's patches with superficial hæmorrhages into these.

We believe that the disease could be considered acute, since there was a definite onset eleven days before admission. It is true that he was a little below par during the preceding year, and this has been true of several cases recently reported as acute. But we do not believe this to be an acute exacerbation of a chronic leukæmia. The low count and small spleen on admission are against that. Sondern's case was "inclined to chlorosis since youth" with slow convalescence from fevers. The onset was that of an acute fever. He had not the throat, or mouth symptoms, nor the enlarged glands, nor the hæmorrhages which so often occur in acute leukæmia, nor was prostration his only symptom. Lazarus[64] states that nearly all cases of acute myeloid leukæmia begin with a mouth or throat infection; ours did not.

His pulse was rather rapid, often dicrotic, of good volume and tension, and the heart practically negative, except toward the end when embryocardia was present.

During the whole course he had a general bronchitis, then on the 16th day a very local pleurisy in the right axilla which soon, on the 19th day, covered both axillæ and much of both backs. As might be expected the respirations became more and more rapid.

At no time was there general glandular enlargement. The tonsils were never enlarged; there was no nasal obstruction, no superficial evidence of enlarged thymus. The posterior and anterior cervicals were just palpable, that was all, until the seventeenth day when were found the infiltrating masses on the inner aspects of both elbows. The liver was at first not enlarged, on admission reaching just to the costal margin, but after the fifteenth day it reached 1.7 cm. below, and was distinctly tender. One cannot say whether or not the spleen was just palpable at first since the abdomen was too rigid for satisfactory palpation, but the edge was not felt nor the dullness increased. On and after the sixteenth day it reached 4 cm. below the costal margin and was very easily felt, hence we are sure had definitely enlarged.

Among the gastro-intestinal features may be mentioned the pains mentioned above, while the shifting dullness in the flanks was a constant and worrying sign. The tongue was very clean at first, and until the eighteenth day. He had often

[57] New York Med. Jour., 1905, Vol. 82, p. 1154.
[58] Loc. cit.
[59] Med. Rec., 1898, Vol. 53, p. 333.
[60] Loc. cit.
[61] Edinb. M. J., 1904, XVI, p. 502.
[62] Lancet, 1905, I, p. 153.
[63] Virchow Arch., 1903, Vol. 173, p. 309.
[64] Deut. Med. Wch., 1905, Vol. XLII, p. 1209.

nausea but no vomiting until the fifteenth day. The diarrhœa was a most troublesome symptom.

The urine of the first two days after admission was normal in amount, of specific gravity 1010, amber color, clear, with no sugar, a good trace of albumin, a few granular casts, and a few pus cells. The Diazo test was negative. After that the total amounts were saved for chemical work.

The hæmorrhagic features were never striking. The first petechiæ were seen on the fourteenth day on the neck, then on the chest, back, arms, and legs. They were small, from 2 to 3 mm. in diameter, never numerous, and might easily have been overlooked. Around the punctures for subcutaneous injections however a subcutaneous hæmorrhage spread for 2 or 3 cms. One or two subcutaneous hæmorrhages appeared in the mouth, and a necrotic area at the base of the middle lower incisor teeth. On the eighteenth day he expectorated about one ounce of blood. Jaundice appeared on the fourteenth day. It was never more than a faint tint.

The eyes, throat, and ears were negative.

Blood.—Red cells. The point most interesting in this case is the absence of severe anæmia. On admission the red cells were 4,300,000. The count rose somewhat later, perhaps due to diarrhœa, but at least there was absence of any great blood destruction, for at the end the count was 4,600,000. There was, therefore, none of the "anæmia progressive and severe" (Billings and Capps), so constant a feature of acute leukæmia. This was, we believed, evidence in favor of its belonging to the myelocytic group, for in the chronic cases this form is not associated with as severe an anæmia as is the lymphocytic; nevertheless if acute myelogenous leukæmia one would expect a more severe anæmia than if chronic myelogenous.[65] This high blood count may throw light on the nature of the two forms of acute leukæmia. Granting both to be myelogenous one supposes that in the lymphoid form the myeloblasts, *i. e.*, the large lymphocytes, predominate (see page 76), in the other the myelocytes (the same cells further differentiated with granular protoplasm). Hence, in the latter, cells of a later generation are involved. It is supposed that these same indifferent cells (large lymphocytes) are directly related to (if not the same as) the parent cells of red corpuscles. It is clear, therefore, if this be true, that in the acute lymphoid type the formation of red cells would be more affected, and so the red count lower, than if the white series was affected at a point below the branching off of the red series. In 14 cases of probably acute myelogeonus leukæmia collected from literature the lowest red counts varied from 2,500,000 to 256,000, mean count 1,500,000. The highest count on admission was 3,132,000. As is seen, no case was found with so high a count as ours.

The red cells were quite normal in appearance, they stained well, there was little poikilocytosis and degeneration. A few normoblasts were found and the early discovery of a typical megaloblast suggested the diagnosis of leukæmia.

In the chronic spleno-myelogenous leukæmia megaloblasts are very common, in the lymphatic, rare. In 8 cases reported of acute myelocytic leukæmia nucleated reds were present in 5, in one 2618 normoblasts per cubic millimeter, and megaloblasts in 2.

The leucocyte count, 12,000, on admission made us doubt that the condition was typhoid. Its constant rise caused repeated search for some pus focus, probably in the liver until the count reached 56,000. Up to that time only the fresh blood had been hastily examined and a polymorphonuclear leucocytosis assumed. But when the count reached 64,800 we made a determined attempt to get a differential count and it was then that the diagnosis was made from the interne's report that the leucocytes would not stain. During the next few days over one hundred futile attempts were made to get a blood film suitable for a differential leucocyte count. For the most part Ehrlich's triple stain was used, but also Hasting's methylene-blue eosin stain, also hæmatoxylin and eosin. Films were heated on the copper bar at the boiling point for periods of from ten minutes to seven hours; others at the spheroidal point for periods of from a few seconds to two hours; others were passed through the flame; the alcohol-ether, the formalin-alcohol, and the methyl-alcohol methods of fixation were also tried. Some films were soaked in ether, others in alkali, others in acid, before heating, and for some smears the blood was diluted with normal salt solution. The results were nearly all about the same; the specimen looked hazy as if seen through a dirty lens; the red cells were always deeply stained, and, except in specimens subjected to very high temperatures, or heated for a long time, were always overstained as if underfixed. That is, after heating even six hours at the boiling point the red cells were of a deep claret color. The nuclei of the lymphocytes were well stained, and as a rule more deeply than normal, but the protoplasm was hardly distinguishable it stained so faintly. A few well-stained polymorphonuclear neutrophiles were found, but of the majority the protoplasm stained a diffuse pale dirty pink and no granules could be made out, while the nuclei stained well, a dark bluish-green, but at times a sea-green. Only two or three polymorphonuclear eosinophiles were seen and these were well stained. In a specimen fixed with methyl-alcohol and stained with Ehrlich's triple stain three typical eosinophile myelocytes were found. Of the large mononuclears and large cells with notched nuclei, the nuclei were for the most part poorly defined and of a light bluish-green color. Of some the protoplasm was uncolored but for the most part took a color from pale pink to a deeper dirty pink. Other films were saved five weeks before fixing, but these gave no better results.

The fresh blood specimens showed a mononuclear leucocytosis, the predominant cell being the large lymphocyte. Many looked perfectly clear of granules, but in the fresh some were clearly granular. These former are the well-known "large lymphocytes" (see page 76). We might suppose that the most of these were non-granular; if so, the case was one of "lymphatic" leukæmia. But that is by no means certain.

[65] Elder and Fowler, loc. cit.

Until the Ehrlich stain was introduced all these were considered as clear cells but Ehrlich showed some of them to be granular and named them myelocytes. It takes a good stain to show the granules of these cells and with the best stains one must count a large number as cells of uncertain nature since it is a matter of technique and of personal opinion whether they are really granular or not.[66] In cases of acute lymphoid leukæmia these cells stain beautifully, nuclei and protoplasm especially in the methylene-blue mixtures while the more differentiated granular cells stain more poorly. The almost uniform refusal of these cells to take any stain may or may not be in favor of the latter. Of the cells which could be recognized a few cells were surely mononuclear neutrophiles and three were eosinophile myelocytes. But the great majority of the leucocytes were represented by a blur in which it was hard to tell the shape of the nucleus or the nature of the protoplasm. The possibilities are the following: first, we may imagine the cells were too young to stain well. Grawitz emphasized the fragility of the young marrow cells. Uskow had shown this also. Special technique is usually necessary to stain embryonic cells. But if so there were surely plenty of older cells which would have stained well, which was not the case. Second, the cells might have been degenerated, undergone lytic processes, to use Wolff's expression. Wolff[67] gives no case to illustrate his points concerning this process. He merely states that, due to lytic processes, often many of the leucocytes won't stain, and since destruction may be as rapid as new formation there may be no apparent increase in leucocytes. The modifications of Romanowski's stain alone, he says, will usually stain these but not always, and in our case this certainly was true. Degenerating cells usually stain beautifully, and surely in our case a few would have been caught when not too degenerated to stain. One might suppose that in our case with the count rapidly rising there would be enough young cells which would take a good stain and allow a fairly interesting differential count, but this was not the case. A very good argument could be written in favor of this degenerating theory, for Weber showed in his case a preponderance of granular myelocytes in the marrow and of non-granular lymphoid cells in the blood. All stages are always found in the blood between granular and non-granular myelocytes. In nearly all cases of lymphatic leukæmia about one-tenth or more of the leucocytes are surely degenerated.

We do not believe this achromatophilia was due to a special quality of the leucocytes but to the blood as a whole, perhaps the chemical nature of the plasma. Our reasons are, that this achromatophilic quality was not of one group but of all; that in some specimens islands stained well, and here a few of all groups of cells could be recognized; and lastly, the red cells stained as if underheated. Specimens were heated for all possible lengths of time hoping to strike the right point, but even extreme heat gave the same picture. We do not believe technique at fault since the stains were well tested, and all modifications of fixation used.

Since so few cells were recognized it is impossible to say what variety of leukæmia it was and yet we suspect it was myelocytic since so many of the cells which could be definitely recognized were granular cells, and of these three were eosinophile myelocytes. When we remember how long one must hunt in well-stained specimens of lymphocytic leukæmia for an eosinophile of any description this occurrence of three myelocytes with those granules would suggest a myelocytic blood. There were also found nucleated reds, normablasts, and a megaloblast, which are rather rare in the lymphocytic form.

Of course a few granular cells do not make the case myelocytic. But in this case the cells whose nature was most easily determined were nearly all granular. Of 12 cases in literature grouped as myelocytic the large lymphocytes varied from 17 to 76%; the small mononuclears, 0 to 34.5%; the neutrophile myelocytes from 10.6 to 60%. Nevertheless the study of the bone marrow is quite in favor of the diagnosis lymphoid leukæmia.

The refusal of the cells to take a stain is our reason for reporting this case. We could find no case in literature just like this, hence report it as a case with almost all the leucocytes quite achromatophilic.

CASE III.—*A case of acute leukæmia (?) with leucopenia, "aplastic leukæmia."*

R. G., age 19 years; female; white; worker in a "sweat shop"; Gen. No. 54419. Admitted April 9, 1906. Died April 15, 1906.

Clinical diagnosis.—Alymphæmic lymphomatosis; or acute pseudoleukæmia; or aplastic anæmia.

The patient was admitted complaining of "headache and giddiness."

The family history was almost negative; both parents were living and well, as were also seven brothers who were all well but one, and he was "short of breath with a little cough," with sputum, which was never bloody. The maternal grandmother died of tuberculosis.

The past history was almost uneventful. As a child she was strong and well, and of all children's diseases had only measles. She never had typhoid fever, malaria, pneumonia, pleurisy, scarlet fever, or diphtheria. As a child she had a bad earache with a discharge, which was not followed by deafness. She never had a chronic cough, no gastro-intestinal symptoms, and no urinary symptoms. She began to menstruate at 14 years of age and had regularly until the past month. She was working hard in a sweat shop under the most unhygienic surroundings.

The present illness began gradually one month ago, with headache and giddiness if she rose suddenly, and on walking. She had not fainted, and had no nausea or vomiting, and no hæmorrhage of any sort. She had been growing paler and had noticed some small lumps in the neck. They were not tender and had had been growing smaller. This headache and giddiness grew worse till April the 2d, when she gave up work and consulted a physician who told her she had mumps, so swollen were her posterior cervical glands. He told her to remain in bed. She remained there two days and then tried to get up, but became very dizzy and for a time blind. Two days ago another doctor was called, who found her very anæmic, with a swollen pale left tonsil, enlarged glands behind the ears, and large glands in the groins and axillæ. He sent her here. [Johns Hopkins Hospital.]

On *physical examination* she presented a striking picture. She

[66] See Billings and Capps, Am. Jour. Med. Sc., 1903, Vol. IX.
[67] Berl. Klin. Wchs., 1905, Vol. XLII, p. 35.

was of large frame and fairly well nourished. The skin was almost white, was moist, and there was no skin rash.

The mucosa of the lips could hardly be distinguished from the skin; she resembled a cadaver. The scleræ were pearly blue.

The tongue was extremely pale and thinly coated.

The teeth were in excellent condition. There was no evidence of bleeding from the gums.

The tonsils were large, especially the right, which was somewhat inflamed, and hence was in striking contrast to the rest of the throat which was very pale. In the crypts were several white cheesy plugs.

The eyes were myopic, and the eyelids were puffy; the fundi and discs were very pale; there were fresh hæmorrhages in each eye.

The vessels of the neck were all full and all the veins pulsated. The thyroid was not enlarged.

The posterior cervical, mastoid, and submaxillary glands were all enlarged, and formed visible tumors. Some of these were 1.5 to 2 cm. in diameter. Those in the anterior triangle were palpable. The enlarged glands were not tender. In both axillæ were very large glands (one was 2 by 3 cm.). The epitrochlears were palpable, about the size of peas. The inguinal glands were about 1 cm. in diameter.

Thorax.—The lungs were clear throughout, except a loud, leathery pleural-friction rub in the right lower front. The heart's point of maximal impulse was in the fourth interspace, 7.5 cm. from the midsternal line. Relative cardiac dulness was not increased. There was at the apex a rough systolic murmur not heard in the axilla; otherwise the sounds were clear. The pulmonic second was accentuated. The pulse was 108 to the minute, very quick and collapsing, of moderate force and tension. The vessel walls were not palpable.

The spleen descended fully 3 cm. below the costal margin in inspiration. Hepatic dulness began at about the fifth interspace, and its edge was easily palpable.

The shins were clear, and the reflexes normal.

Blood, April 9.—Hæmoglobin, 16% (Fleishl); red corpuscles, 1,144,000; white corpuscles, 3800; large mononuclears, 43%; small mononuclears, 39%; polymorphonuclear neutrophiles, 14%; eosinophiles, 1%; myelocytes, 0.2%; unidentified, 2.5%.

One normoblast was found in counting 500 leucocytes.

April 11.—White corpuscles, 3600.

April 12.—Hæmoglobin, 18%; red corpuscles, 940,000; white corpuscles, 3700. Blood cultures taken to-day remained sterile.

April 14.—The patient looked even more exsanguine. There was now a faint yellow tint to the scleræ, but the face and body showed none of the saffron hue, or lemon-yellow tint seen in the primary pernicious anæmia. The glands were diminishing somewhat in size. Under the left clavicle the breath sounds were rather harsh, and many clicking râles were heard following inspiration. A few râles were heard down the left front and axilla. The pulse was distinctly water-hammer in quality, and the wave audible with the stethescope even at the wrist. Respiration was deep and rapid as if "air hunger" were present. The relative hepatic dulness began in the right mammary line at the upper margin of the sixth rib, and extended to about 3 cm. below the costal margin. The spleen now could only just be felt; it was much smaller than on admission. On the lower extremities were seen many subcutaneous hæmorrhages, which were on and below both knees and on the dorsum of the feet. The palms of the hands and soles of the feet were of an orange hue. The shins were clear; there was no œdema of the ankles; the reflexes were normal. The Widal test was negative.

April 14.—The patient was suffering from marked air hunger and from frequent attacks of nausea. There was a loud friction rub in the left back, and the right axilla and back.

Blood examination.—Red corpuscles, 724,000; hæmoglobin, 13%; white corpuscles, 1920.

April 15.—The patient died early this morning, with marked respiratory distress. She looked completely exsanguine.

The urine varied from 620 to 2250 ccs. in 24 hours, and its color was pale yellow though slightly turbid. The specific gravity was from 1011 to 1017, the reaction acid, with no sugar, no albumin, and only a few squamous (vaginal) epithelial cells in the sediment.

The temperature was continuous, between 101° and 103° at times, reaching 105° on one occasion. On these days the variations of the two-hour chart were not over one degree. The pulse ran exactly parallel to the temperature, from 120 to 130, and the respirations varied from 24 to 28. The most interesting feature of this case was the constancy of temperature, pulse and respiration.

Unfortunately no autopsy could be performed.

When this case was admitted we confidently expected to find it one of acute leukæmia, but to our surprise leucopenia was present. There were all the general features of acute leukæmia; the severe anæmia, the cachexia, the hæmorrhages, the general glandular enlargement, the large liver and large spleen; but the leucocyte count was only 3800 per cubic millimeter, 1630 of which were large mononuclears, 1500 small mononuclears, 530 polymorphonuclear neutrophiles, 38 eosinophiles, 7 myelocytes, and 95 unidentified. There was even the pleural friction rub not rare in acute leukæmia. What was very interesting was the dimunition in the size of lymph glands, liver, and spleen, simultaneous with the drop in the red and leucocyte counts. The course was fairly acute, not over five weeks at the longest.

Cases somewhat similar to this have been reported under a variety of names, among which are: acute pseudoleukæmia, acute Hodgkin's disease, lymphatic pseudoleukæmia, aleukæmic pseudoleukæmia, sublymphæmic lymphomatosis, aleukæmic leukæmia, aplastic leukæmia, and chloroma. Unfortunately no autopsy was obtained, hence the most important evidence for a diagnosis could not be obtained.

Pseudoleukæmia is a most convenient term. It means a condition itself not clear, which simulates leukæmia and yet is not. It can be anything else providing the resemblance is striking and that anything else is itself without better diagnosis. It was used for Hodgkin's disease until this was shown by Reed to be a distinct condition; of many cases of tuberculosis adenitis until the introduction of the tuberculin reaction; of cases of splenomegaly until splenic anæmia and Banti's disease were separated; of lymphosarcoma and malignant lymphoma until the practice of removing glands for diagnosis was common (and now the pathologists may sometimes be wrong). All that is left is a theoretically possible group of cases which clinically resemble leukæmia; that is, they have severe anæmia, cachexia, weakness, the hæmorrhagic diathesis, often the enlarged lymph glands, liver and spleen, and yet a leucocyte count, normal quantitatively and qualitatively. Some go one step farther and say that the histological picture of the marrow should be that of leukæmia. We believe this last specification is too stringent and doubt if any such case is on record (Reed). The word pseudoleukæmia

would then have lost its value and a better name could be given to so exact a clinical and anatomical picture. By pseudoleukæmia all we mean is that, go as far as we can, although this may not be far, as in this case, the condition resembles leukæmia and yet is not, since the blood picture is absent. But there is always a chance that the blood picture was formerly leukæmic or later will be, and it is because we cannot exclude these possibilities that we use this term. The term pseudoleukæmia is a confession of our ignorance. We are quite sure, for example, that a case which is now Hodgkin's disease never has been and never will be leukæmia except as a condition new to that patient.

But ours was not a case of acute pseudoleukæmia, since the blood formula was anything but normal, was, in fact, truly leukæmic, with over 1600 cells per cubic millimeter of a group not represented in normal blood at all. We did not remove a gland for microscopic examination, hence cannot be sure that it was not Hodgkin's disease, although the blood formula would exclude that also. Also it is indeed rare in Hodgkin's disease for the lymph glands to recede.

Hand [68] reported a case of aleukæmic leukæmia in a boy two and a half years old. He was admitted six weeks after the onset with swollen feet, puffy eyelids almost closing the eyes, with subcutaneous, submucous, and subconjunctival hæmorrhages, epistaxis, and hæmatemesis. The liver reached 6 cm. and the spleen 3 cm. below the costal margins. The lymph glands were generally enlarged. The red cell count was 1,390,000, hæmoglobin 23%, leucocytes 6300 (small lymphocytes 85%, large 4.75%, polymorphonuclears 8.85%). Unfortunately there was no autopsy.

Ours could have been a case of acute lymphatic leukæmia at a later stage, for Holst [69] reported one the successive counts of which were 93,000, 130,000 (large lymphocytes 96%, polymorphonuclear neutrophiles 3.10%, small lymphocytes 0.9%), 58,000, and one day before death, 1600 (polymorphonuclears 50%, large lymphocytes 10%, small lymphocytes 40%).

Jeanselme and Weil [70] report an interesting case of three weeks' duration with leucocyte count, 4400, polymorphonuclears 22%, small mononuclears 58.5%, large mononuclears 15%, plasma cells 4%, but with the marrow of acute leukæmia. Neumann (also Wolff and Pappenheim) believed that in leukæmia we have a process which can attack the spleen, liver, lymph glands, or the bone-marrow. So long as the first three organs are affected the blood remains normal and the condition is a pseudoleukæmia. When first the bone-marrow is invaded, the hard inelastic bony capsule forces the sarcomatous tissue to invade the vessel walls and hence cells press into the blood current, and leukæmia begins. So long as the endothelium of the vessels is still intact the condition is "alymphæmic pseudoleukæmia"; [71] while the entry of cells into the blood stream is only slight, "sublymphæmic lymphomatosis," the lymphatic pseudoleukæmia of Pinkus; when many cells press in, the condition is "lymphatic leukæmia." [72] According to this scheme our case with normal count yet large numbers of large lymphocytes would be one of "sublymphæmic lymphomatosis." Wolff [73] reports a case under the heading "aplastic leukæmia" which resembles our Case III in many ways. He states that there was aplasia of bone-marrow but qualitatively the changes were those of lymphatic leukæmia. The liver was large (six fingers breadths below the costal margin), the spleen small, a few glands were slightly enlarged, and the leucocytes varied from 3000 to 5000. The anæmia was severe and progressive, reaching 500,000 red cells. Wolff says we can recognize aplastic leukæmia intra vitam by the large percentage of large lymphocytes together with the low total count, and especially by the progressive severe anæmia without signs of regeneration. If no large lymphocytes are present one can still make the diagnosis from the relatively large number of lymphocytes. Our case would certainly correspond to this blood picture, for the mononuclear non-granular cells were 82% of the total 3800 leucocytes, and of these 43% were large, while the anæmia in our case was certainly severe enough. But unfortunately we do not know what the bone-marrow looked like.

Aplastic anæmia is very similar to aplastic leukæmia if one judge from the blood alone. A recent case will illustrate this. The woman, 48 years of age, had had a typhoid fever of terrible severity and with many complications including hæmorrhages, thrombus of axillary vein, bed sores, pleurisy with effusion, acute lobar pneumonia and a psychosis. After all this hard course we were congratulating ourselves that recovery was now possible, the temperature remaining normal, but it seemed as if the blood could not regenerate. The red cells had fallen from 4,448,000 to 2,500,000 and then 1,582,000; the hæmoglobin from 55% to 37%, to 25%; and the leucocytes at three times were 4000, 6200, and 5300. It seemed as if the bone-marrow had failed utterly to replenish the blood, hence no new cells were furnished, and the anæmia progressed as the old were removed. She died on the 95th day of the illness, and 22 days after the temperature had reached normal for the last time. We have seen severe malaria behave in a somewhat similar manner.

A diminution in size of lymph glands, liver, and spleen coincident with the fall in the count is sometimes reversed as in a case of acute lymphatic leukæmia in the wards a few years ago. The patient was seen in September with large

[68] Arch. of Pediatrics, Dec., 1905.

[69] Loc. cit.

[70] Pédiat. prat., 1904, II, p. 52; and Bull. et mém. d. Soc. méd. des hôp. de Paris, 1904, XXI, p. 185.

[71] Türk, Wien Klin. Wchs., 1903, Vol. 16, p. 1073.

[72] See Banti, Centralb. f. Allgem. path. und path. Anat., 1904, Bd. 15, p. 1.

[73] Berl. Klin. Wchs., 1905, Vol. XLII, p. 35.

glands but normal blood, and a diagnosis of Hodgkin's disease made. He was admitted December the 25th with the lymph glands much smaller, and the leucocyte count 133,400. His course was very severe with hæmorrhages, and he died January 19 with the white count about the same, but the lymph glands smaller still. In this case as the count rose the visible hæmatopoietic organs diminished in size. Kuhnan and Weiss [74] report a case in which also this point was present.

All things considered we think, in the absence of an autopsy, that "acute aplastic leukæmia" is the best diagnosis we can make.

[74] Zeitsch. f. Klin. Med., 1897, Vol. 32.

THE NECESSITY OF A MORE UNIFORM NOMENCLATURE OF DISEASES FOR STUDY AND TEACHING.[1]

By Thomas Morgan Rotch, M. D.,

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To the physician in general practice, whose busy days are spent in the care of the sick and their treatment, it matters little whether or not a practitioner in some distant city calls a disease by the same name as he, according to his locality or to his previous instruction, is accustomed to and satisfied with. To him, also, it is of little moment whether a number of different diseases which he meets with are called by the same name. It not only does not matter to him, but even the suggestion that the terms which he is using are meaningless and incorrect is met with mild scorn as a subject too trivial upon which to waste the time and thought of one whose life is made up of honest endeavor and untiring work for the relief of suffering humanity. If, however, he would but think for a moment, and look at the question from a little different point of view, he might at least be willing to aid those who are endeavoring to untangle a labyrinth of misleading words which, as mere relics of past ignorance, clog the wheels of progress, in that they do not represent the great advances which have been made in the medical knowledge of the present day. He would then also see that many of the ancient titles mean the ancient supposed knowledge of what are now known to be exploded theories, and that to use them means the unnecessary continuation of false ideas. But even if such a practitioner should be willing to acknowledge that he had been giving a number of different diseases the same treatment because he had learned to classify them under one name, he would naturally draw attention to the fact that physicians in general throw all the responsibility of names upon the instructors whom, in the various universities, they have paid to teach them how to diagnosticate and treat diseases and that in receiving that instruction they rightly look to the instructor to at least give them the correct name under which they are to carry out such instruction. Still further, if, attracted by the name and experience of a medical author, he should purchase a book to instruct him, he expects from the index to turn to the page where the disease he is seeking light on is under its own definite heading. It never occurs to him that that very heading is a delusion and a snare, the use of which is unworthy of the brain which has evolved the perhaps brilliant description of the disease which follows. If it is allowed that his reasoning is correct and that such an unfortunate state of affairs actually exists, he will then probably understand how important a matter it is for the curing of disease and the saving of life in his own practice, to join with those who would force upon the attention of instructors and authors that their work is but half done when their teaching is stultified by a false nomenclature.

It is, however, these very teachers who realize, as no one else can, the difficulties which arise when they attempt to study and make use of the writings of others who from their experience are fully competent to throw light on a given subject, and yet whose investigations become doubtful and obscure because the uncertainty is always arising as to whether under the name of the disease they are describing they mean one or a number of diseases, or because they are using a different name for the disease than is used by the one who is seeking information, and who, therefore, hesitates to accept such information. If the teacher finds difficulties arising in his investigation of a subject owing to his not understanding the latest work of others on that subject, how much is the difficulty increased when he endeavors to impart the latest knowledge to the student, for he feels that he is not doing justice to the subject, and knows that the student needs correct names to aid him in grasping the true relationship of diseases to each other. What I have just said, though in the main true, is, of course, greatly exaggerated, and exaggerated purposely to show what may occur under certain instances and what in the future will inevitably occur more frequently unless we adopt a more uniform and rational nomenclature. It is especially for the sake of the medical student, the general practitioner, and ultimately the patient, that by means of systematic headings, approved and adopted by the leading centres of teaching, diseases should be studied and referred to under uniform headings representing exactly what is known about them.

I have for many years been impressed with the belief that the subject of a classification for clinical purposes was an

[1] An address read by invitation of the Johns Hopkins Medical Society at the Johns Hopkins Hospital, January 7, 1907.

important one, and one which ought to be dealt with by teachers, as they can best appreciate the value of such a subject. The pathological classification has year by year been changed and improved and kept up to the later researches by the pathologists; the terms for physical diagnosis have been revised and improved by the clinical teachers, but the nomenclature of diseases has not kept pace with our knowledge of them.

The revision of a classification is extremely difficult, the difficulties being especially realized by those who have attempted it. In 1894 Dr. Forchheimer and myself, as a committee of the American Pediatric Society, presented a classification of Diseases of the Mouth in Early Life. It was adopted by the Society and went no further than to appear in our own books. In the same year Dr. Holt and myself presented a classification for Gastro-Enteric Diseases in Early Life on partly an anatomical and partly a clinical basis: it was not accepted. In the following year, however, I felt so firmly that it should be adopted that I brought it up again and it was passed by the Society, but with some strong opposition. I immediately had it introduced into the teaching of the Pediatric Department at Harvard where it has been taught ever since. It was never used to any extent by individual members of the Pediatric Society or anywhere else.

It is a curious fact that the profession clings to old names by preference. It has seemed to me self-evident that to really make any headway in a classification, the great teaching centres, such as Baltimore, Philadelphia, New York, Chicago, and Boston, should work together and agree on provisional classifications which can be changed from time to time according as any new etiological discoveries warrant us in so doing.

A uniform classification means uniform teaching: it means that Johns Hopkins can come to Harvard and Harvard to Johns Hopkins for an additional degree without the applicant being handicapped by such an unnecessary obstacle as not understanding the terms used in his examination, resulting from the teachers in the two universities using different terms, perhaps satisfactory to themselves, but puzzling for the student.

Even if only a beginning could be made by reclassifying one or two subjects where it was needed most, much good would come of it, for the teachers would then understand what great practical aid would result from an advanced classification for the clinical work in all diseases. With this idea in view I have in conjunction with my colleagues in the Pediatric Department at Harvard made a new classification of Gastro-Enteric Diseases in Early Life on an etiological basis, believing that no classification of these diseases can be made satisfactory for clinical work excepting from an etiological standpoint. This classification has been approved by the American Pediatric Society and adopted by the Pediatric Department of Jefferson. I believe, however, that for any permanent good which can come from it, it should be criticized and mutually revised by the different universities; and then if satisfactory to all, brought into universal use as an example of what can be done. Those who teach the clinical medicine of the different periods of life, whether it be infancy or childhood, adult life or old age, should each present for the approval of the others the classification for the period of life which they are especially studying and teaching.

I think that after I have spoken in detail of this classification which I am presenting to you to-night, that you will agree with me that a classification when possible should be on an etiological basis. We believed this 14 years ago, but at that time found it impossible and therefore were forced to place our classification partly on an anatomical and partly on a clinical basis, which, however, was a great advance on the old and unmeaning names used before.

In endeavoring to bring the teaching centres to agree on a uniform classification, we should present, first, a *primary* classification the details of which can later be worked out by the individual teacher and perhaps finally adopted by all. If at first we go beyond this primary classification, my experience tells me that we shall fail to come together. The sample classification, therefore, which I am about to give you, must be considered primary or approval of its etiologic basis will not be universally given.

Although the diseases of the gastro-enteric tract form perhaps the most important division of pediatrics, there is none in which there is so much confusion and diversity in the terminology employed. Almost every clinical condition is described by a number of different terms, some of which are relics of obsolete theories and others the products of modern research. As an example of this multiplicity of synonyms, one clinical condition in infancy is spoken of by the following different names: summer diarrhœa, acute gastro-enteric intoxication, gastro-intestinal catarrh, gastro-enteritis, cholera infantum, mycotic diarrhœa, fermental diarrhœa and acute intestinal indigestion. This confusion is a source of difficulty both to students and to those engaged in scientific research. The student, in order to study intelligently the work of various observers who employ a varying terminology, must burden his mind with many synonyms. The investigator has difficulty in describing his results in terms which shall be generally intelligible.

Much of the difficulty is due to the fact that at no time has the classification of these diseases been founded upon any definite basis. Such terms as gastritis, ileocolitis, and catarrh are based upon pathologic anatomy; other terms, such as indigestion and nervous diarrhœa, are based on etiology; while still others, such as gastralgia and diarrhœa, are merely names of symptoms. In the classification adopted by the American Pediatric Society in 1894, the gastric and enteric disorders respectively were first divided into functional and organic on an anatomic basis. Then the functional disturbances were divided into acute and chronic on a clinical basis, while the organic diseases were divided into inflammatory and non-inflammatory on an anatomic basis. The further subdivisions of these groups were made usually on an etiologic basis.

These three bases, the clinical, anatomic, and etiologic, are all employed in the classification of diseases in general, in the

endeavor to fit clinical descriptions to postmortem findings, and to etiologic factors. The clinical basis is obviously unscientific, and should only be adopted in those diseases which have neither a well-recognized etiology nor a constant pathologic anatomy. This is not the case with the diseases of the gastro-enteric tract, many of which have a recognized etiology. Classification on an anatomic basis is absolutely impossible from the fact that while some conditions show no anatomic changes on postmortem examination, others show a great variety of changes, and a marked lack of correspondence between the clinical picture and postmortem findings. Diseases of widely different etiology and symptomatology may show the same changes postmortem, while diseases of a constant etiology and symptomatology may show postmortem conditions varying from no demonstrable lesion to the very gravest.

So strongly has this been impressed upon me, especially when I have undertaken to teach the students at Harvard what we know concerning diseases of the gastro-enteric tract in infancy and early childhood, that before attempting to describe the etiology and symptoms, I at once speak of the anatomical findings as a whole.

I show them how much is known by the pathologists—how carefully described and classified pathologically are the lesions which may be found postmortem in the gastro-enteric tract—I tell them that, with comparatively few exceptions, it is impossible to tell clinically whether any or all of these lesions are present, and that as the pathologist has in a number of cases been unable to give us an anatomical picture to correspond to the etiology they clinically are of little use to us. I then present to them for inspection some of these lesions found in young subjects, without corresponding symptoms, so as to impress upon them that to name the diseases after these lesions is misleading—that is, the lesion must always be one of the secondary details in a nomenclature of the gastro-enteric tract.

I will show a few of these lesions on the screen, but it is of course to be remembered that they are of early life and therefore are the more likely not to be accompanied by corresponding clinical symptoms. They represent a great variety of intestinal lesions and are impressive as suggesting that a number of causes may produce any one of them and that no one cause has been found to produce them all; also that grave as are many of these lesions, they in no way aid in the diagnosis and so far as naming the disease anti-mortem is concerned are entirely without value.

The following lesions were then shown on the screen:

No. I. *Girl*, 8½ *Years*.—Tubercular Ulcers of Colon. 2 months before death, chills; temperature, 103°; prostration. Diarrhœa showing nothing. Nothing on physical examination except enlarged glands. *Post mortem*, lungs normal; large sloughing ulcers of cœcum and colon. Tubercle bacilli found.

No. II. *Girl*, 2¾ *Years*.—Tubercular Ulcer—Small Intest. Diarrhœa occasionally for a year and convulsions. No lesions which could be determined during life.

No. III. *Girl*, 2 *Years*.—Typhoidal Ulcers of Colon. Marked Thickening and Ulceration of Peyers' Patches and of Solitary Follicles.

In this case the irregularity of the temperature curve and the prominent symptoms of cerebro-spinal irritation rendered the diagnosis of typhoid so obscure that it was not suspected until a few days before death.

No. IV. *Young Infant*.—Hyperplasia of Lymph Follicles.

Lesions marked and simulate closely the hyperplasia of Peyers' Patches seen in typhoid; only slight diarrhœa.

No. V. *Girl*, 3 *Years*.—Non-Ulcerative Follicular Inflammation. Simple Hyperplasia of Lymph Follicles.

Symptoms; excessive vomiting following improper food. No intestinal symptoms. Death in 5 days.

No. VI and VII. *Boy*, 2 *Years*.—Non-Ulcerative Follicular Colitis. Solitary follicles enlarged, most prominently in upper third of intestine; no ulceration; Peyers' Patches markedly swollen.

Continued high temperature, 104° F. Slight diarrhœa, 2 weeks; discharges showing nothing marked. Symptoms mostly of cerebral type, and abdominal symptoms not prominent.

No. VIII. *Infant* 16 *Months*.—Ulcerative Follicular Colitis. No tubercular lesions found. Extensive follicular ulcerations of colon.

Occasional attacks of diarrhœa for 3 months. No other marked clinical symptoms.

No. IX. *Girl*, 3 *Months*.—Acute Ulcerative Catarrhal Colitis. Lymph follicles enlarged but not ulcerated. Colon showed numerous ulcerations, which were simply necrotic.

Emaciated and fretful. No vomiting. Temperature normal or sub-normal. One large yellowish-green movement daily.

No. X. *Girl*, 3 *Months*.—Inflammation of Follicles and Surrounding Parts of Colon with Extensive Ulcerations of Colon. Process had Gone on to Necrosis.

No acute symptoms; 6 to 8 greenish, loose discharges in 24 hours; slight vomiting. Temperature, 95° to 101°. Failed and died in about 5 weeks.

No. XI. *Boy*, 6 *Months*.—Chronic Catarrhal Ulcerative Follicular Colitis. Pigmented Follicular Ulcers of Colon.

No especial abdominal symptoms. Wasted away and died in a few days after entering hospital.

No. XII. *Child*, 3½ *Years*.—Pseudo-membranous Colitis, confirmed by microscopic examination. Other organs normal (entire length of colon affected). Much reduced after pertussis. Diphtheria, and for 10 days a slight amount of diarrhœa, but no pain or tenesmus.

These cases show how inadequate are symptoms not only for the diagnosis of lesions, but often how insufficient are they to even enable us to diagnosticate any lesions whatever.

The modern tendency is toward an etiologic basis of classification. The progress of bacteriology is constantly separating certain clinical pictures, and labelling them with the name of the specific causative agent. Therefore, it would seem advisable, if possible, to classify the diseases of the gastro-enteric tract upon an etiologic basis. It is not possible to use terms which in every case suggest the etiology, as certain conditions have been so long known by definite names which cannot be discarded. But it is possible to choose among synonyms that name which is most suggestive of the etiology. More important still, it is possible to arrange these diseases in definite

groups, on an etiologic basis. The following classification is suggested:

DISEASES OF THE GASTRO-ENTERIC TRACT.

- **Gastric**
  - Developmental — Malpositions, Malformations . . . . Pyloric stenosis.
  - Non-Infectious
    - Mechanical . . . . Contraction, Dilatation.
    - Ulcers . . . . . Peptic.
    - New growths.
    - Functional . . . . Nervous vomiting, Recurrent (periodic) vomiting, Indigestion.
    - Traumatic . . . . . Corrosive gastritis.
  - Infectious . . . Gastritis.
- **Enteric**
  - Developmental — Malpositions, Malformations.
  - Non-Infectious
    - Mechanical . . . . Dilatation of colon, Volvulus, Intussusception, Hernia, Fissure, Prolapse, Hæmorrhoids.
    - New growths.
    - Functional
      - Incontinence,
      - Constipation,
      - Nervous Diarrhœa,
      - Indigestion — Intestinal — Duodenal, Deficient secretion, Fermentation.
  - Infectious . . .
    - Infectious diarrhœa — Dysentery, Cholera infantum, Other organisms.
    - Proctitis,
    - Appendicitis,
    - Fistulæ.
    - Intestinal worms.

The diseases are divided into three groups, developmental, non-infectious, and infectious. The further subdivisions of the non-infectious groups are based as far as possible on the origin of the condition. The conditions of mechanical and traumatic origin need no further explanation, nor do the new growths and peptic ulcer. The word functional is used, not as in the old classification, to mean the antithesis of organic, but rather to mean that the origin of the disease is a disturbance of function, from various causes. Nervous diarrhœa and nervous vomiting suggest nervous influences. Recurrent or periodic vomiting is a definite clinical type of an origin which, though unknown, is probably definite. Indigestion means disturbance of the function of digestion, in either the stomach, duodenum, or intestine.

The term gastritis, although an anatomic one, is retained, for the reason that there is no satisfactory synonym suggesting the etiology.

On the other hand, the term ileocolitis is discarded as being inappropriate for the name of a disease. Ileocolitis is found postmortem in a great variety of different clinical conditions. Moreover, certain cases in which ileocolitis is found have been relegated to the category of such specific infections, as typhoid fever and tuberculosis. The term infectious diarrhœa is chosen as most suitable for describing the infections of the intestine, for the reason that it suggests both the etiology and the principal symptom.

Under the diseases of the stomach there will be found a close and obvious fitting of the clinical picture to the term used in describing it. Under the diseases of the intestine it was necessary to subdivide the cases of indigestion into duodenal and intestinal, in order to fit well-recognized clinical types. The acute duodenal indigestion represents the well-known clinical type often spoken of as catarrhal jaundice, or gastroduodenitis. Chronic duodenal indigestion is the clinical type usually spoken of by the same name, with its characteristic clinical symptoms of nausea, occasional vomiting attacks, abdominal pain, loss of weight, coated tongue, prominent abdomen, and clay-colored movements.

In the division of intestinal indigestion, it is necessary to further subdivide into two clinical types, the primary cause of which is the same, disturbance of the digestive function. In the first type the symptoms are due to simple functional disturbance, the secretions being deficient, or at least insufficient to perform the work required of them, with consequent diarrhœa from irritation of undigested masses. This type, from deficient secretion, is characterized by an absence of toxic symptoms, especially of fever, and by movements containing curds, or undigested masses, but not notably foul. In the second type the symptoms are due to deficient secretion plus bacterial fermentation. It is characterized by the frequent occurrence of brief initial fever and toxic symptoms, and by green movements of foul odor.

A clear distinction is drawn between those cases which show fermentation from saprophytic bacteria in the intestinal contents, and those in which there is true infection of the tissues with parasitic bacteria. The former cases may show serious symptoms as the result of toxic absorption, but are nevertheless due primarily to disturbance of the digestive function, and are, therefore, classified as the fermentation type of intestinal indigestion. The latter cases are classified under the heading infectious diarrhœa.

The cases classified as infectious diarrhœa clinically resemble true infections. They are characterized by persistent fever, with its attendant symptoms, and by the frequent early appearance of blood and mucous in the movements. From recent bacteriologic research it is probable that the majority of these cases are due at least in part to infection with the Bacillus dysenteriæ. Nevertheless, since it has not been proved that this organism is the sole etiologic factor in intestinal infection nor that it is causative in all the cases of this clinical type, the term infectious diarrhœa is preferable to infantile dysentery. The latter term may be reserved for those cases in which the finding of the Bacillus dysenteriæ in the movements, and of an agglutinin of this organism in the blood, proves that this organism is actually causative in the individual case.

Cholera infantum is so distinct and has been so long recognized as a clinical type that the term is retained as describing one form of infectious diarrhœa, the etiology of which, though still unknown, is probably a definite form of infection.

It is hoped that the classification suggested and outlined will prove advantageous both for teaching and for future scientific investigation; for teaching, because the student will need to carry in mind only certain definite etiologic groups. He must in any case know what is known of the etiology of these conditions. When he meets with a condition described under

a synonym, his knowledge of its etiology will at once enable him to interpret it correctly, and classify it properly. For convenience in teaching, conditions of similar anatomic and clinical descriptions, but different etiology, have been placed in such a way as to follow one another, and thus the distinctions between them can be made more clear to the student, without confusing his mind by describing a disease of entirely different symptomatology in between. Thus corrosive gastritis, of traumatic origin, follows immediately after indigestion, of functional origin, and is followed in turn by the gastritis of infectious origin. Also, the functional diseases of the intestine are placed immediately before the infectious, and their subdivisions arranged in such a way as to bring out sharply the distinction between the various forms of diarrhœa, the descriptions of which follow one after another.

It is hoped that this classification will be advantageous to the scientific investigator, because future investigation is to be mainly in the domain of etiology. The arrangement of the diseases of the gastro-enteric tract in definite groups, on an etiologic basis, separates at once those conditions of which the etiology is known, from those of which the etiology is partially or wholly unknown. This will simplify the description of the results obtained in the future.

I appeal to you who represent the most advanced ideas in medicine extant, and are looked up to as the source from which emanates the best medical teaching in this country, to aid your sister teaching centre—Harvard—to impress upon the teachers throughout the world the necessity of an advanced and uniform nomenclature.

BENJAMIN RUSH, AS MATERIALIST AND REALIST.[1]

By I. Woodbridge Riley, Ph. D.,

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Dr. Benjamin Rush, of Philadelphia, was the most conspicuous of the American medical materialists of the eighteenth century. Born of English stock in Pennsylvania in 1745, at school under the Reverend Samuel Finley, the later head of Nassau Hall, then at Princeton itself under President Samuel Davies, he learned the rudiments of medicine from Dr. John Redman. Obtaining his medical degree in Edinburgh University, walking the London hospitals, and helped by Franklin to study in Paris, he returned to America in 1769 and became in turn professor of chemistry in the Medical College of Philadelphia, physician-general of the continetal army of the middle department, and professor of the institutes of medicine in the new University of Pennsylvania.

Subjected to the varying influences of Anglo-American deism, Scottish realism, and British and French materialism, Rush's philosophical remains range from an undergraduate transcription of the metaphysical system of Dr. Davies, and a translation at the age of seventeen of the *Aphorisms of Hippocrates,* to his *Thoughts on Common Sense,* and a final volume on the *Diseases of the Mind.* It was in regard to this last work that he made the interesting statement that the diseases of the brain should be watched, since they often produce discoveries of the secret powers of the mind; like convulsions of the earth, which throw up metals and precious stones, they would otherwise have been unknown forever.[2]

As in his speculations Rush was a living compromise between various divergent schools of thought, so in his numerous public activities he was a personal paradox: in politics a signer of the Declaration, yet a maligner of the military genius of Washington; in education an agent in bringing President Witherspoon to Princeton and President Nisbet to Dickinson, yet a philistine as regards the study of the classics; in philanthropy an opponent of capital punishment and of slavery, yet a believer in the most drastic measures to stamp out the yellow fever; in medicine a pioneer in psychiatry, yet the originator of a species of phrenology. The dual nature of the man is outwardly shown in his portrait, which represents him in a pensive and yet a self-conscious attitude, his head in his hand but one eye cocked on the observer. So, from his works and his looks Rush may be judged to be rather profuse than profound,—a hard-headed philosopher, dealing in what he was pleased to call the practical metaphysics of the mind. Mere theories did not disturb him. When at Edinburgh he was thrown with David Hume, but no traces of that subtle sceptic are to be found in his thought. At home he received from Jefferson a confidential copy of the *Syllabus of the Doctrines of Jesus,*[3] but that did not shake his orthodox beliefs.

In a word, Rush was an eclectic. He took what he wanted and left what he did not like. Consistency was not his, for he was influenced in turn by deism, realism, and materialism. The influence of the first appears in the teleological trimmings of his system, the moral bearings he gave to his physiology and psychology. Like Hartley, he was not content with examining man's frame, but extended his observations to his duty and his expectations. Likewise in his realism the good doctor was wont to pick and choose. For common sense he found use at first rather in a political than in a philosophical sense. He had suggested the term as a title for Thomas Paine's revolutionary pamphlet of 1775, but by 1791 he writes that he had long suspected the term to be

[1] A chapter from a forthcoming volume on American Philosophy, read at a meeting of the Johns Hopkins Historical Club, December 10, 1906.

[2] Purnell MS., p. 50.

[3] Jefferson Works, Ford. ed. 8, 223. Letter to Rush, April 21, 1803.

applied improperly to designate a faculty of the mind.[4] Here he will not repeat the accounts which have been given of it, from Cicero and Berkeley to Hobbes and Hume, but will confine himself to differing with Reid's account of the matter. Instead, then, of considering it a faculty or part of a faculty, possessing a quick and universal perception of right and wrong, truth and error in human affairs,—he will define it simply as opinions and feelings in unison with the opinions and feelings of the bulk of mankind. From this definition it is evident that common sense must vary with the progress of taste, science, and religion. Thus it is contrary to common sense to speak in favor of republicanism in Europe or of monarchy in America; it is contrary to common sense to use opium, bark, mercury, or the lancet, but agreeable to it to revenge public and private injuries by wars and duels; common sense in Great Britain and the United States is in favor of boys spending four or five years in learning Latin and Greek, whereas it is contrary to right reason to teach them words before they are taught ideas. In fine, to say that a man has common sense, is to say that he thinks with his age and country, in their false, as well as their true opinions. After all that has been said in its favor, one cannot help thinking that it is the characteristic only of common minds. Had this common sense depended upon the information of the five external senses, one would have no difficulty in admitting Dr. Reid's account of it. But to suppose it the first act of the reason and afterwards to suppose it to be universal is to contradict everything that history and observation teach us of human nature. And yet in the progress of knowledge, when the exact connection between the senses and reason is perfectly understood, it is probable that the two will be in unison with each other, but this unison as in the case of vision—where the reason connects the distance of objects with the evidence of the eyes,—must be the result only of experience and habit.[5]

To judge from this diatribe against the "doubtful faculties of taste and intuition,"[6] Rush must have suffered from that overdose of realism which he got in his undergraduate days and while a student at the Scottish capital. The reaction sent him over into the English materialism. The transition between the two is exactly marked by the title of his best known essay, the *Influence of Physical Causes upon the Moral Faculty*. Delivered before the American Philosophical Society in 1786, this exhibits a vocabulary borrowed from speculative Edinburgh, but an application suitable to utilitarian Philadelphia. The moral faculty, to borrow the term of Beattie, may be called the moral sense of Hutcheson, the sympathy of Adam Smith, the moral instinct of Rousseau, the regula regulans of the schoolmen; it may be a native principle, a capacity in the human mind of distinguishing good and evil, a faculty quick in its operations, and like the sensitive plant acting without reflection,—it may be all these things, and yet, at the same time, be subject to physical influences.

Do we observe a connection between the intellectual faculties and the degrees of consistency and firmness of the brain in infancy and childhood? The same connection has been observed between the strength as well as the progress of the moral faculty in children. Do we observe instances of a total want of memory, imagination, and judgment, either from an original defect in the stamina of the brain, or from the influence of physical causes? The same unnatural defect has been observed, and probably from the same causes, of a moral faculty. A nervous fever may cause the loss not only of memory but of the habit of veracity. The former is called amnesia, the latter unnamed malady will compel a woman, be she even in easy circumstances, to fill her pocket secretly with bread at the table of a friend.[7]

For instances and reasonings like these, drawn from his own experience and practice, Rush has been designated the father of psychiatry in America.[8] In venturing upon this untrodden ground the doctor confesses that he feels like Æneas when he was about to enter the gates of Avernus, but without a Sibyl to instruct him in the mysteries before him. He therefore begins with an attempt to supply the defects of nosological writers by naming the partial or weakened action of the moral faculty *micronomia,* its total absence *anomia.* But to name these derangements is not to explain them; they may be caused not only by madness, hysteria, and hypochondriasis, but also by all those states of the body which are accompanied by preternatural irritability, sensibility, torpor, stupor, or mobility of the nervous system. It is in vain to attack these accompanying vices, whether of the body or of the mind, with lectures upon morality. They are only to be cured by medicine and proper treatment. Thus the young woman, previously mentioned, that lost her habit of veracity by a nervous fever, recovered this virtue as soon as her system recovered its natural tone.[9] Furthermore, it makes no difference whether the physical causes that are to be enumerated act upon the moral faculty through the medium of the senses, the passions and memory, or the imagination. Their action is equally certain whether they act as remote, predisposing, or occasional causes. For instance, the state of the weather has an unfriendly effect upon the moral sensibility, as seen in the gloomy November fogs of England; so does extreme hunger, as in the case of the Indians of this country who thus whet their appetite for that savage species of warfare peculiar to them. Again, the influence of association upon morals is strong. Suicide is often propagated by the newspapers and monstrous crimes by the publication of court proceedings. And as physical causes influence moral, so do they influence religious principles. Religious melancholy and madness will

[4] Thoughts on Common Sense, p. 249.
[5] Ibid., pp. 251-4.
[6] Purnell MS., p. 81.
[7] Moral Faculty, pp. 6, 7.
[8] W. Pepper, Journal of the American Medical Association, April 26, 1890, p. 6, note 2.
[9] Moral Faculty, p. 26.

yield more readily to medicine than simply to polemical discourses or casuistical advice.[10]

In this presentation of the influence of physical causes upon the moral faculty, its advocate anticipates the objection raised to it, from its being supposed to favor the materiality of the soul. And yet he does not see that this doctrine obliges us to decide upon the question of the nature of the soul, any more than the facts which prove the influence of physical causes upon the memory, the imagination or the judgment. The writers in favor of the immortality of the soul have done that truth great injury, by connecting it necessarily with its immateriality. The immortality of the soul depends upon the will of the Creator, and not upon the supposed properties of spirit. Matter is in its own nature as immortal as spirit. It is resolvable by heat and mixture into a variety of forms; but it requires the same almighty hand to annihilate it, that it did to create it. It would be as reasonable to assert that the basin of the ocean is immortal from the greatness of its capacity to hold water, or that we are to live forever in this world, because we are afraid of dying,—as to maintain the immortality of the soul from the greatness of its capacity for knowledge and happiness, or from its dread of annihilation.[11] On another occasion and in a less figurative way, Rush strove to disentangle the popular confusion between these two concepts. The writers to whom he now specifically refers are Plato and Cicero, Locke and Priestley. Regarding the nature of the mind, he says, the two first suppose it to be immaterial and independent of the body. Locke supposes it to consist of a matter, exquisitely fine, and connected with the body; that it is incapable of existence without the body, but that it does not perish with the body. Priestley supposes that there is no such thing as a mind either material or immaterial. With this meager reference to the Northumberland advocate of the homogeneity of man, the student who took these notes passes with unconcealed delight to a doctrine apparently different from all the variant forms, ancient and modern. Dr. Rush, he explains, believes that the mind is immaterial, that it can exist independently of the body, and that there is no necessary connection between the immateriality and immortality of the mind, the one being a divine attribute, the other a divine gift.[12]

Returning from this digression, the immaterialistic materialist comes to a defence of his main proposition,—the universal and essential existence of a moral faculty in the human mind. He apologizes for presuming to differ from such a justly celebrated oracle as Locke, yet holds that the latter has confounded this moral principle with reason, just as Lord Shaftsbury has confounded it with taste, since all three of these faculties agree in the objects of their approbation, notwithstanding they exist in the mind independently of each other.[13] One may admit with Locke that some savage nations are totally devoid of the moral faculty, yet it will by no means follow that this was the original consitution of their minds. As well might we assert, because savages destroy their beauty by painting, that the principles of taste do not exist naturally in the human mind. It is with virtue as with fire. It exists in the mind as fire does in certain bodies, in a latent or quiescent state. As collision renders the one sensible, so education renders the other visible. It would be as absurd to maintain, because olives become agreeable to many people from habit, that we have no natural appetite for food, as to assert that any part of the human species exists without a moral principle, because in some of them it has wanted causes to excite it into action, or has been perverted by example. There are appetites that are wholly artificial. There are tastes so entirely vitiated, as to perceive beauty in deformity. There are torpid and unnatural passions. Why, under certain unfavorable conditions, may there not exist also a moral faculty, in a state of sleep, or subject to mistakes?[14] Ending with one of the author's habitual rhetorical flourishes this passage leaves an impression of weakness. But while it makes the moral principle a poor thing, incapable of affecting positive results, leading to no where in particular, the suggestion as to artificial and vitiated tastes opened a fruitful line of inquiry, leading indirectly to the last and most important work on the diseases of the mind.

Having considered the influence of physical causes upon the moral faculty Rush next takes up "the influence of physical causes in promoting an increase of strength and activity of the intellectual faculties of man." Delivered as an introductory lecture to his students in 1799, it exhibits a growing tendency towards materialism, together with a more cautious avoidance of metaphysical speculations. The writer confines himself only to those agents which increase the quantity of mind, leaving the causes which lessen it to a later pathology. He then passes by the knotty questions of the theoretical nature of the mind, deeming it sufficient for his present inquiry to believe that all its operations are the effects of bodily impressions, a belief according with the axiom of the schools—"nihil est in intellectu quod non prius fuit in sensu."[15]

In employing the trite maxim of sensationalism and treating the mind as if it were a pint measure, the speaker is but adapting his remarks to the capacities of his hearers. Desiring to present facts intelligible to the youngest student of medicine, he brings in anecdotes which savor more of natural history than of mental philosophy. Such are the bits of information that Jonathan Edwards rode a trotting horse to stimulate his thoughts; that Joseph Priestley, in order to strengthen his faculties, used to write upon every subject which he wished to understand perfectly; that in republics mental vigor is increased by the frequency of general elections. In citing these miscellaneous cases with all their triviality Rush, nevertheless, has a serious purpose. It is to calculate the degrees of vigor, and the number and exility of motions

[10] Moral Faculty, pp. 42, 47.
[11] Ibid., p. 19.
[12] Purnell MS., p. 81.
[13] Moral Faculty, p. 17.
[14] Moral Faculty, pp. 15, 16.
[15] Intellectual Faculties, p. 88.

which the mind is capable of receiving. It is by the exercise of the body and the collision of our intellects, by means of business and conversation, that we impart to them agreeable and durable vigor. The effects of this action and reaction, in making addition to the intellects and knowledge, lead us to admit the assertion of Condorcet that the time will come, when all the knowledge we now possess will appear to the generations that are to succeed us, as the knowledge now possessed by children appears to us. . . . From what has been delivered, gentlemen, it appears that the enlargement and activity of our intellects are as much within our power as the health and movements of our bodies.[16]

This is the characteristic conclusions of an introductory lecture to the study of medicine. To judge from certain manuscript notes of one of the doctor's pupils the others resemble it in being full of wise saws and modern instances: *e. g.,* the brain is like the lower limbs, if exercised it lasts; as the body is stimulated by air, so the mind is stimulated by motives; the faculties may be compared to a well-organized government: the memory and imagination to the House of Representatives, the understanding to the Senate, in which the transactions of the House of Representatives are examined, the moral faculties to the courts of justice, the conscience to the court of appeals.[17]

The works of the Philadelphian thus far are popular and superficial. With their abundant illustrations, from classical allusions to local anecdotes, they bear out John Adams' estimate of Rush as an elegant and ingenious body, but too much of a talker to be a deep thinker.[18] But this stricture can only in a measure be passed upon the next production of Rush's middle period, the *Three Lectures upon Animal Life.* The author is here more modest in his claims, in proportion as he is more thorough in his results. He disclaims being the source of the great and original conception upon which they are founded, confessing that he has done little more than carry the hod to assist in completing a part of the fabric of which the foundations were already laid.[19] It was while a student in the University of Edinburg in 1766 that he heard Dr. Cullen deliver the opinion that the human body is not an automaton, or self-moving machine, but is kept alive and in motion by the constant action of stimuli upon it. This opinion, which Rush repeated in one of his own lectures as early as 1771, he now enlarges into three general propositions concerning the human body, namely: that every part of it is endowed with sensibility; that it is a unit, a simple and indivisible quality of substance; and finally, that life is the effect of certain stimuli acting upon the sensibility and excitability, which are extended in different degrees over every external and internal part of the body. These stimuli are as necessary to its existence as air is to flame. Included, moreover, in animal life are motion, sensation, and thought. These three, when united, compose perfect life. The term motion is here preferable to those of oscillation or vibration, as employed by Dr. Hartley in explaining the laws of animal life, because it is more simple and better adapted to common apprehension.[20]

To this modified materialism the American now proceeds to attach a peculiar form of realism. In opposition to the Hartleian leaning toward monism he sets a form of pluralism: man is not a machine whose parts, however complex, are homogeneous, but he is rather a number of entities acted upon by a variety of forces. Or as Rush puts it, in addition to the external stimuli like heat and light, and the internal like the action of the brain, and the pulsation of the arteries, there are the intellectual stimuli arising from the exercises of the faculties of the mind itself. Thus the imagination acts with great force upon the body, and the passions pour a constant stream upon the wheels of life.[21]

Like a good realist the author has hypostatized the faculties. Yet he does not leave them hovering in mid air as mere empty quiddites. To the mind of the materialist, thought itself is the effect of stimuli acting upon the organs of sense and motion. Furthermore, the exercises of the faculties of the mind have a wonderful influence in increasing the quantity of human life. They all act by reflection only, after having been previously excited into action by impressions made upon the body. This view of the reaction of the mind upon the body accords with the simplicity of other operations in the animal economy. Finally, common language justifies the opinion of the stimulus of the understanding upon the brain, hence it is common to say of dull men, that they have scarcely ideas enough to keep themselves awake. And so, contrary to the picture of the Indian character drawn by Rousseau, their vacant countenances are to be attributed to the effects of the want of action in their brains from a deficiency of ideas. Again, atheism does violence to the mental faculties by robbing man of his most sublime beliefs, abstracting his thought from the most perfect of all possible objects. This is demonstrated by the theophilanthropists, who, after rejecting the true God, have instituted the worship of nature, of fortune, and of the human race.[22]

In these curious illustrations of a quantitative conception of mentality Rush's psychology threatens to degenerate into a sort of arithmetic of the mind, for beside the minus side in his table of values there is the plus. Thus the whole animal machine may be set in motion by the love of money, as was shown in the Philadelphia panic of 1791, when speculation over the scrip of the United States Bank excited febrile diseases in three of the doctor's patients. Similar mental stimuli are furnished by political conditions; many facts prove animal life to exist in a larger quantity in the enlightened and happy state of Connecticut, in which republican liberty has existed

[16] Intellectual Faculties, pp. 114, 117.
[17] Purnell MS., p. 96.
[18] Works, 2, 427.
[19] Animal Life, Preface, p. v.
[20] Animal Life, pp. 5-7.
[21] Ibid., p. 6.
[22] Ibid., pp. 19, 20, 67.

above one hundred and fifty years, than in any other country upon the surface of the globe.[23]

These strange generalizations, concerning the larger aspects of animal life, do not prevent the author from taking up the smaller phenomena, the minuter influences in the psychic life. Speaking of slight sounds which it is not necessary should excite sensation of perception, in order to their exerting a degree of stimulus, he adds: there are a hundred impressions made daily upon the body, which from habit are not followed by sensation; the stimulus of the blood upon the heart and arteries probably ceases to be felt only from the influence of habit. It is unfortunate that we forget what passed in our minds the first two or three years of our lives. Could we recollect the manner in which we acquired our first ideas, and the progress of our knowledge with the evolution of our senses and faculties, it would relieve us from many difficulties and controversies upon this subject. Perhaps this forgetfulness by children of the origin and progress of their knowledge might be remedied by our attending more closely to the first effects of impressions, sensation, and perception upon them as discovered by their little actions, all of which probably have a meaning as determined as any of the actions of men or women.[24]

By piecing together the broken hints of his authorities, from Leibniz on minute perceptions to Reid on how the infant faculties begin to grow, Rush in a measure advances the genetic point of view. But that suggestive method is again unfortunately spoiled by a quantitative misconception. In his attempt to be precise the materialist verges toward an accurate arithmetic rather than a trustworthy psychology. In other words, the American realist, following the lead of the Scotch, has attempted to obtain a distinct and full history of the mind of the child; but the result is scarcely "a treasure of natural history." Nor is the succeeding disquisition, which seeks to establish the principle that animal life in every species depends on the same causes as in the human body. But what is of interest here is the cautious conclusion reached by the former dogmatist: From a review of what has been said of animal life in all its numerous forms and modifications, we see that it is as much an effect of impressions upon a peculiar species of matter, as sound is of the stroke of a hammer upon a bell, or music of the motion of a bow upon the strings of a violin. I exclude, therefore, the intelligent principle of Whytt, the medical mind of Stahl, the healing powers of Cullen, and the vital principle of John Hunter as much from the body, as I do an intelligent principle from air, fire, and water. . . . It is not necessary to be acquainted with the precise nature of that form of matter which is capable of producing life from impressions made upon it. It is sufficient for our purpose to know the fact. It is immaterial moreover whether this matter derive its power of being acted upon wholly from the brain, or whether it be in part inherent in animal fibers. The inferences are the same in favor of animal life being the effect of stimuli and of its being as truly mechanical as the movements of a clock from the pressure of its weights. . . . Should it be asked what is the peculiar organization of matter, which enables it to emit life, when acted upon by stimuli, I answer, I do not know.[25]

Notwithstanding his agnostic conclusion regarding man as a machine, Rush has something to say on the practical application of his doctrine to metaphysics and morality. It enables us to reject the doctrine of innate ideas, and to ascribe all our knowledge of sensible objects to impressions acting upon an innate capacity to receive ideas. Were it possible for a child to grow up to manhood without the use of any of its senses, it would not possess a single idea of a material object; and as all human knowledge is composed of simple ideas, this person would be as destitute of knowledge of every kind, as the grossest portion of vegetable or fossil matter.[26] Again, the account which has been given of animal life furnishes a striking illustration of the origin of human actions by the impressions of motives upon the will. As well might we admit an inherent principle of life in animal matter as a self-determining power in this faculty of the mind. Motives are necessary not only to constitute its freedom, but its essence; for without them there could be no more will than there could be vision without light, or hearing without sound. It is true they are often so obscure as not to be perceived, and they sometimes become insensible from habit, but the same things have been remarked in the operation of stimuli; and yet we do not on this account deny their agency in producing animal life. In thus deciding in favor of the necessity of motives to produce actions, I cannot help bearing a testimony against the gloomy misapplication of this doctrine by some modern writers. When properly understood it is calculated to produce the most comfortable views of the divine government and the most beneficial effects upon morals and human happiness.[27]

Thus far the system of Rush exhibits the three familiar marks of materialism, namely, a phenomenalistic view of substance, a sensationalistic of perception, a deterministic of volition. Now there are added certain incongruous elements. Seeking to apply his doctrine to the sphere of theology the Philadelphian embellishes it with remnants both of an earlier deism and even of that Edwardean occasionalism, which had not been obliterated when Rush was an undergraduate at Princeton. The best criterion of the truth of a philosophical opinion, he continues, is its tendency to produce exalted ideas of the Divine Being and humble views of ourselves. The doctrine of animal life which has been delivered is calculated to produce these effects in an eminent degree. It does homage to the Supreme Being as the governor of the universe, and establishes the certainty of his universal and particular providence. Admit a principle of life in the human body and we open a door for the restoration of the old Epicurean or

[23] Animal Life, pp. 62, 64.
[24] Ibid., p. 11.
[25] Animal Life, pp. 73, 74, 75.
[26] Ibid., p. 78.
[27] Ibid., pp. 79, 80.

atheistical philosophy, which supposed the world to be governed by a principle called nature, and which was believed to be inherent in every kind of matter. The doctrine I have taught cuts the sinews of this error, for by rendering the continuance of animal life, no less than its commencement, the effect of the constant operation of divine power and goodness, it leads us to believe that the whole creation is supported in the same manner.[28]

To this last observation of the last lecture on *Animal Life* Rush at some later period added a disquisition on *Liberty and Necessity.* As extracted from his unpublished *Letters and Thoughts,* and containing an erased passage of no small originality, it will bear generous quotation:

Is it not absurd to talk of *past* or *future* when we speak of the knowledge of the Deity? Can anything be *past* or *future* to a being who exists from eternity to eternity? Are not past, present, and future to *Him*, one eternal *now?* Is not time a finite idea only, and past and future knowable only to finite beings? May not the moral actions of men then have appeared as complete to the Deity at the creation as the *material* world? I see the objects of a plain before me as distinctly as if I were near it. My view of it has no influence on its form or distance; the same probably occurs to the Deity with respect to pre-existing actions. Imperfect man by *memory sees* past events—a wonderful power in a finite mind! May not a perfect being see future events in the same manner? They all have an existence in the eternal mind. *There is nothing* truly *new* in actions, any more than in truths *under the sun.* There can be no contingency with the Deity—all is fixed and immutable with Him; cause and effect, *motive* and *action*, creation and preservation, all one simple object and act. . . . The perfections of the Deity require this solution of this doctrine. *Prescience* is only a human term, but, like many others applied to the Deity in accommodation to our weak capacities. Prophecies are to Him things present; to us things to come—hence their great accuracy. It is improper and dishonorable to His glorious Oneness in existence as well as nature. It is impossible matters should be otherwise. Succession belongs only to man. God can do and know nothing in succession. So far for necessity. But all this is compatable with the most perfect liberty. The knowledge of God of actions flows from a perfect knowledge of the union between cause and effect in creation. All is still free. An artist can tell from the construction of a machine exactly its strokes, etc., without touching it after its wheels are set in motion, although he still upholds it in his hand. We still live, move and have our being in *God*. . . . Nor does this idea destroy man's responsibility. He is still free. His liberty is essential to the necessity—otherwise his action would have no moral nature and could not be the object of pardon, and for this purpose alone evil existed. It must be free to be a crime, and crimes existed, not for a display of vindictive justice in endless punishment, but for the display of love in justice in endless and and universal happiness. This removes all the fears and difficulties about moral necessity. It was necessary that man should fall—it was likewise necessary that he should be *free*, or he could not have fallen. Liberty and necessity are, therefore, both true, and both necessary to advance in due consistency all the glorious attributes of God. This union of liberty and necessity may be illustrated by a simple example: [1. I walk on the deck of a ship. Here is one free motion—the helmsman steers the ship in the direction in which I walk, and yet I am not influenced by his helm, not he by my walking; we both direct our course the same way—he, by pointing the bow of the ship, makes me keep the same course with him, but without my knowledge or his influence over my will. 2. I resolve to take a walk to an adjoining village. This is the first act of my will. On my way I forget the original act of my will and occupy it upon twenty other objects, none of which have any connection with the first. Here then is a will within a will.] I require a perfect knowledge of a man's taste in building, and then convey secretly into his hands a plan of a house. Every act of this man in building this house is foreknown by me, and yet no influence is exercised over his will. Here is necessity and liberty united.[29]

This is a reactionary document, betraying the conflict between the spirit of orthodoxy and the spirit of free inquiry. As a projected addition to the essays on *Animal Life* it explains the opposition to the revival of the ancient "atheism" and also the closing confession that the author feels as if he had waded across a rapid and dangerous stream. The figure is a good one; it exhibits Rush as conscious of the drift of his speculations. And yet in opposing his dualistic occasionalism to a monistic hylozoism, he was but vainly struggling against the tendency of materialism toward a single unitary principle,—the reduction of both mind and matter to modifications of the same common substance.

That tendency as regards anthropology, if not cosmology, is manifested in the opening passage of the next lecture *On the Utility of a Knowledge of the Faculties and Operations of the Mind to a Physician.* Man is said to be a compound of soul and body. However this language may be in religion, it is not so in medicine. He is, in the eye of a physician, a single and indivisible being, for so intimately united are his soul and body, that one cannot be moved without the other.[30] This is the doctrine of the homogeneity of man. In substituting it for his earlier dualism, Rush was undoubtedly influenced by his friend Priestley, who had read the Philadelphian's earlier lectures and called them sublimely speculative.[31] But while this supplementary lecture begins with a decided monistic turn, its force is speedily dissipated by the intrusion of pluralistic arguments,—the dividing up of an indissoluble being into separate faculties. Among these are included not only memory, imagination, and understanding, but in addition, the principle of faith, the passions, the moral faculty, conscience, and a sense of deity.[32] Disregarding Locke's warning against supposing the faculties to stand for some real beings in the soul,[33] Rush has weakened his initial plan by the assumption that there are minds within a mind, extra agents within a single agent. Nevertheless, this complexity has its practical side. Like the modern assumption of selves split off from the self, multiple personalities within one body, it calls attention to the intimate relations subsisting between the psychical and the physical, and leads to a fruitful study of the abnormal and pathological. Or, as Rush himself puts it, a knowledge of the faculties and operations of mind fur-

[28] Animal Life, p. 81.

[29] Ridgeway MS., Letters and Thoughts, pp. 28-30.

[30] Lecture XI, 1805, p. 256.

[31] Cf. Bolton, Scientific Correspondence of Dr. Priestley, letters of Aug. 8, 1799, and Jan. 27, 1802.

[32] Utility, p. 257.

[33] Human Understanding, Bk. 3, chap. 21, § 6.

nishes many useful analogies by which we are enabled to explain or illustrate the actions of the human body. Like the will and its motives, these actions do not occur without the influence of external and internal impressions, association and habit; indeed, as pathology shows, the different faculties of the mind when unduly exercised act specifically upon certain systems and parts of the body.[34] Moreover, this science of mind can be applied to abnormal as well as normal. Since the operations of the understanding act upon the brain and vary with sex, rank, profession, climate, season, time of day, they will explain morbid phenomena of the body and mind, particularly the causes of dreams, trances, phantasms, and supposed voices; all of which have been superstitiously ascribed to supernatural influence.[35] For example, unfavorable changes discovered in diseases in the morning are often the effect occasioned by the disturbing dreams of the night before; while the pain of a surgical operation is often lessened by telling the patient that the worst part of it has been performed.[36] Having touched on suggestive anæsthesia some forty years before the application of material anæsthetics in America, and having mentioned the influence of the passions in curing the diseases of the body, the lecturer now maintains that their efficacy is much greater in curing the diseases of the mind. To compose and regulate the passions, there are to be found means ranging from the physical influence of music to the removal of painful associations of ideas, as when a fever, caught while out gunning, was cured by removing the gun from the ill man's room.[37]

It is at this point that Rush's underlying quantitative conception of mentality again crops out. In his *Animal Life* he had spoken of the tempers and dispositions of the mind as if they were so many psychical quarts and pints. Here the faculties and their operations are presented as if they formed a parallelogram of forces, a framework of calculable energies. Thus, by opposing a new and fresh to an exhausted passion, by combining two passions against one, by giving a passion, that has operated in a retrograde course, its natural direction, madness, from the influence of the passions upon the understanding and will, has often been cured, without the aid of any other remedy.[38] Granted that this way of looking at things may appear strange, it still has its advantages. It renders the science of mind an exact science, not a chimerical and uncertain thing. While it bore the name of metaphysics, and consisted only of words without ideas, of definitions of nonentities, and of controversies about the ubiquity of spirit and space, the materiality and immateriality of mind,—it deserved no quarter from the rational part of mankind. But the science I am now speaking of is as real as any of the sciences that treat upon matter, and more certain and perfect than most of them. Note the changes and improvements that have taken place in the theories of every branch of what is called physical science within the last two thousand years. Very different is the state of phrenology, if I may be allowed to coin a word to designate a science of the mind. Most of the leading opinions and observations of Locke, Condillac, Hartley, and Reid may be found in the writings of Aristotle and Plato, and discoveries in this science are now as rare as they are in anatomy. The reason of this certainty and near approach to perfection is obvious. The mind is the same now as it was in the time of those illustrious Greek philosophers, and of course exhibits the same phenomena in all its operations to the moderns, that it did to them. It is moreover always present with us, and always subject to our observations. It requires no excursions from home, no apparatus of instruments or agents, to develop its operations; hence there is nearly the same coincidence of opinion concerning them that there is of the qualities of bodies that act upon the senses.[39]

This is the concluding passage of the lecture of 1805. It is interesting and eloquent but at the same time disappointing. Rush's analogies sound like original discoveries and promising anticipations; but they are neither. His hints regarding suggestive therapeutics were to be traced back to the Zoönomic philosophy, his suggestions regarding the localisation of cerebral functions became involved in phrenology. The Philadelphian appears to have utilized the word a decade before Hunter applied it to the system of Gall and Spurzheim.[40] Unfortunately his use of this "history of the faculties of the human mind," as he elsewhere defined it,[41] betook of the nature of a pseudo-science. In a lecture of this period on *Dreams*, he said: whatever part of the brain is affected the dream that takes place is of that nature,—different parts of the brain being allotted to the different faculties and operations of the mind. Thus, if the moral part is affected, we dream of committing crimes, at the very thought of which we shudder when awake.[42] So, too, the closing part of the lecture defending a knowledge of the faculties is neither original nor sound. Rush confesses that he is not singular in considering such lectures as a branch of physiology, these faculties having been considered by Dr. Haller in his large work, under the title of *sensus interni*.[43] While the American, then, did service in differentiating his science of mind from speculative metaphysics, yet he did not succeed in carrying it over into the safer field of psycho-physics. His method was vitiated by the obstinate misconception that reflection is the chief avenue to knowledge. Here he might be contrasted with Franklin, follower of no subjective school, but believer in any objective experiment. One can imagine what the latter would have made of Judge Hopkinson's suggestion regarding the composition of a scale of pleasurable sensations by the fingers, analogous to the musical scale, by means of objects of dif-

[34] Utility, p. 258.
[35] Ibid., p. 259.
[36] Ibid., p. 263.
[37] Ibid., 267.
[38] Ibid., pp. 264-5.
[39] Utility, pp. 271-2.
[40] Cf. Baldwin's Dictionary of Philosophy and Psychology, *sub verbo*.
[41] Lecture XII, on Hippocrates, p. 295.
[42] For an adverse opinion of Gall's Craniology, cf. Medical Repository, 11, 438, N. Y. 1808.
[43] Utility, p. 272.

ferent degrees of softness and smoothness."[44] Rush considered his friend's thought an ingenious one, but did not carry it into execution. For this his earlier training was to blame. For instruments of precision he preferred simple introspection. On the verge of possible discoveries realism bandaged his eyes.

Notwithstanding this preference for inward over outward observation, hints for a primitive experimental psychology are given in the ensuing lectures *Upon the Pleasures of the Senses and of the Mind.* Having described the offices of the senses, the author now intends to enumerate their pleasures, and to inquire into their causes, that is, into the changes which are produced in the nerves by the sensation of pleasure.[45] Of these two inquiries the former, as might be expected, leads to a perfect medley of facts and fancies. Among the senses of touch are given the sensation of perfect health which the Germans call self-feeling;[46] the joy of fear which the Indians experience after surviving a bloody victory; the sensation of tickling which partakes of both pain and pleasure. An illustration of the pleasures of sight is Hogarth's line of beauty which delights the eye because it consists of an unbroken curve; an instance of the pleasures of sound that of the winds, rains, and streams of water—all doing homage to the ears of man. More important than this enumeration of the pleasures of the senses, is the inquiry into the accompanying changes produced in the nerves. The fundamental proposition here is that the pleasure we enjoy from music is derived from a certain order and relationship of vibrations, which are excited in the ear, to each other; while the pain we feel from discord is produced by the want of order, or relationship, in the vibrations which strike the ear.[47] Rush had once decried the Hartleian theory of vibrations, here he makes a particularly unhappy application of it. Assuming that the pleasure we derive from our ears is ascribable to impressions and vibrations of a peculiar kind, and pain to an excess or dissonance of similar impressions, he states that it is from this organ that he borrows his analogies to explain the causes of pleasure and pain in all the other organs.[48] For example, the pleasure derived from contemplating a beautiful face is produced by certain harmonious motions in the retina of the eye; the pleasures of the table by a harmony in the relations of the aliments, provided, of course, that there is no mixture with indelicate toasts and bacchanalian songs; the pleasures of smell by a difference in harmony imparted to the nerves of the nose by the scale of odors. Here magnolia may be said to resemble bass, the rose tenor, the wall-flower the treble tones! In fine, all the pleasures of the senses being produced from greater or less degrees of harmony analogous to the vibration of musical sound, our bodies may be compared to a violin; the senses are its strings; everything beautiful and sublime in nature and art is its bow; the Creator is the hand that moves it; and pleasure, nearly constant pleasure, their necessary effect![49]

To these ridiculous analogies the other materialists made more or less direct answer. Buchanan, of Kentucky, protested against turning the human system into a violin; Cooper, of South Carolina, ironically mixed a sort of vibratory punch in which the spirits and the lemon were blended in harmonious proportions. But aside from Rush's figures of speech, attributable to the pedagogue's propensity to make matters clear to the meanest intelligence, the lecture on the *Pleasures of the Senses* contained a number of valuable observations, summed up in the form of laws of sensation. Such were the statements that some pleasures are increased, others lessened by repetition; that motion in the organ increases the sensitivity of touch; that the loss of the use of one sense often increases the pleasures of another, the blind enjoying music more than those who possess their eyesight; finally, that we are able to receive only a single sensation in our minds at once, the impressions of yellow and blue, for example, exciting the green color.[50] These laws, for one thing, lead Rush to disagree with the theory of Edmund Burke, presented in his treatise on the *Sublime and Beautiful,* that relaxation is so extensive a source of pleasurable sensations. Rather should one conclude that motions of a moderate degree of force, and in regular order, constitute pleasure; and that motions in excess, and out of order, constitute pain.[51] Or, to use an obvious simile, pleasure may be compared to a clear stream of water flowing with rapidity through a straight and narrow channel; pain to the same stream rendered turbid by flowing with accumulated velocity and in every possible direction.[52]

Rush's laws of sensation appear the more safe as they are the less specific. When freed from such latent metaphors as the senses being so untuned by diseases as to emit no tones of pleasure, they stand as suggestive contributions to current knowledge. Such are the closing remarks that the pleasures of the senses are of short duration; that they are of limited nature as to their degree—no ingenuity being ever able to raise them so high as to perfectly satisfy the mind; finally, that they are so nearly related to pain that they often terminate in it. In the last of these summary negations the materialist has well nigh formulated a law of diminishing return applicable to the psychical field. But herein his first aim is apparently not so much to uphold exact science as practical piety. He means to show that numerous and delightful as are the pleasures of the senses, they have their alloy, and yet that, in these evils, heaven is still kind,—since we are taught by them to aspire to more sublime and durable pleasures of the mind, the subject of the next lecture.[53]

In this supplementary treatise the author pursues the same order as before. He enumerates the pleasures of each of the

[44] Pleasures of the Senses, p. 409.
[45] Pleasures of the Senses, p. 399.
[46] Cf. Rush's essay on the "Manners of the German Inhabitants of Pennsylvania."
[47] Pleasures of the Senses, p. 428.
[48] Ibid., p. 432.
[49] Pleasures of the Senses, pp. 424-5.
[50] Ibid., pp. 425-6.
[51] Ibid., p. 432.
[52] Ibid., p. 428.
[53] Ibid., p. 436.

faculties; inquires into their proximate cause; and concludes with some general remarks. As another introductory lecture the subject must be made interesting at all hazards. So, under the first of these topics there appears the customary mixture of rhetoric and anecdote. By the memory we command, as it were, the suns that have gone down to rise again; by the understanding we gain the most delicate and sublime pleasures. The nature of this may be conceived from the fact that Mr. Rittenhouse fainted upon perceiving the transit of Venus on the third of July, 1760. Again, the pleasures of the association of ideas are so peculiar a nature that an old African slave, who saw a lion conducted as a show through New Jersey, was transported with joy, being carried back to the days of his boyhood in his native country.

Having pointed his moral with provincial tales, and brought the subject down to his hearers, Rush returns to his original quest,—the higher hedonism of intellectual pursuits. Here he emphasizes the pleasures of the will as consisting in contemplating the mysterious union of free agency and necessity in all its operations. We are barely pleased with what we understand; but the exercise of admiration is necessary to our intellectual happiness, and this can be employed only upon subjects which are removed beyond our comprehension. While we thus contemplate, with a delightful wonder, the union of free agency and necessity, we derive pleasure from a sense of each of their respective operations. The pleasure we enjoy in free agency is felt in the sacrifices that we make for the attainment of liberty and in reflecting that we are masters of ourselves. The pleasure we enjoy in a belief in the will acting from necessity is in disposing us to view the hearts of all the men that move our world by their powers or their talents, as under the direction of a wise and good being; and it assures us that all the events that relate to our individual happiness, whether from moral or physical causes, are in his hands and that his hand is in every event. I am aware that I dissent from two popular and rigid sects of philosophers and divines, in thus admitting the truth of the opinions held by each of them. But an exclusive belief in either of them, so far from being attended with pleasure, is calculated to excite misery and despair. I repeat, therefore, what I said formerly in speaking of the operations of the will, that both opinions appear to me to be alike true; and that we act most freely when we act most necessarily, and most necessarily when we act most freely.[54]

Here are the paralogisms of the pure reason considered not as mutually exclusive but as actually complementary. And nothing could better exemplify Rush's habit of looking on both sides of the shield at once. The only ground and justification for reaching such a cross-eyed conclusion lay in his private paper on *Liberty and Necessity*. But this, as previous inspection showed, left the matter decidedly undecided, the best argument being a suppressed simile. Equally unsatisfactory is the author's treatment of the problem of personality, incidentally subsumed under the pleasures of consciousness. Identity, it is asserted, may be conceived of from a single fact. There never was a man who was willing to change his own mind for that of any other person, however willing he might be to exchange his condition, limbs, and face with him.[55] In thus generalizing from a single instance Rush seems to ignore the perversions of consciousness. It was apparently not until later that he met with the anomaly of double personality in the reputed two minds of the somnambulist. This one-sidedness is exceptional, for in treating of his favorite faculty, the moral sense, Rush takes a broader outlook and includes both the extreme and abnormal manifestations of this activity. He holds that the intensity of the pleasures derived from this source is so great, that it may destroy bodily pain,—as in the case of the primitive martyrs to Christianity, who had joys even in the flames of fire. And the perversions of the same faculty are so remarkable that it may become a veritable idiosyncrasy,—as in the case of the Parisian in the reign of Robespierre, who declared that the most delightful music he ever heard was the sound of the guillotine.[56]

Having enumerated the pleasures of the mind and some of their perversions, the author comes to his second inquiry—their proximate cause. This may be summed up in a few words. They are the effects of impressions of a certain definite or moderate degree of force, accompanied with motions of a regular or harmonious nature in the brain and heart and communicated by them to the mind. This is to be inferred from dissections, which discover marks of undue or irregular excitement in the brain and of rupture or disorganization in the heart, where death has been the consequence of an excess of intellectual or moral pleasure.[57] In his extreme zeal for palpable results the materialist has assumed a cause too great for its effects. His contention, however, may serve as a fitting transition to his last and most extended work of philosophic interest, the *Medical Inquiries and Observations upon the Diseases of the Mind*. Published in 1812, at the solicitation of the author's pupils, this volume is said to be a supplement to materials already collected, a set of new principles founded upon old facts.[58] Unfortunately for his claims to originality Rush neglects to refer to the books from which he drew these facts. Then, too, he repeats many of his former borrowings. Again are the faculties lengthily enumerated, and a special plea made for the sense of deity according to Lord Kames; again are they defined, in the manner of Haller, as internal senses, depending wholly upon bodily impressions to produce them. Indeed, it said after the fashion of Locke, as well might we attempt to excite thought in a piece of marble by striking it with the hand, as expect to produce a single operation of the mind in a person deprived of the external senses.[59] With these resemblances to former doctrines there yet goes a difference; there is a similar combination of realism and sensationalism, but

[54] Pleasures of the Mind, pp. 441-3.

[55] Pleasures of the Mind, p. 449.

[56] Ibid., p. 445.

[57] Ibid., p. 452.

[58] Observations, Preface, p. v.

[59] Ibid., p. 11.

the materialism is slightly modified. The Hartleian figures of speech are dropped and a safer generalization adopted. No longer is the body compared to a musical instrument, or the senses spoken of as untuned by diseases so as to emit no tones of pleasure. Refusing then, like Priestley and like his own colleague Frederick Beasley, of the University of Pennsylvania, to commit himself to any specific theory of vibrations, Rush carries out his previous implications in the following postulate: all the operations in the mind are the effects of motions previously excited in the brain, and every idea and thought appears to depend upon a motion peculiar to itself. In a sound state of the mind these motions are regular, and succeed impressions upon the brain with the same certainty and uniformity that perceptions succeed impressions upon the sense in their sound state.[60] Except for an unwarranted assumption of the priority of the physical over the psychical, Rush's thesis might almost be counted a rough formulation of the theory of psycho-physical paralellism. At the least it is a practical working hypothesis, or, as he puts it, a system of principles that shall lead to general success in the treatment of the diseases of the mind.[61]

Having considered the faculties and operations of the mind, it is in order to inquire into the proximate cause of intellectual derangement. Here the American alienist reviews the erroneous opinions on this subject from the ancient notion that the liver is the seat of the trouble, to the modern belief in favor of madness being an ideal disease. The former theory Rush had met in his lecture on the *Opinions and Modes of Practice of Hippocrates;* the latter, as to madness being purely psychical, he objects to for three reasons: first, because the mind is incapable of any operations independently of impressions communicated to it through the medium of the body; second, because there are but two instances upon record of the brain being found free from morbid appearances in persons who have died of madness; third, because there are no instances of primary affections of the mind, such as grief, love, anger, or despair, producing madness until they had induced some obvious changes in the body.[62]

In this same thorough manner the doctor next examines the remote and exciting causes of intellectual derangement. Briefly put, these are of two classes: first, those that act directly upon the body, as malconformations and lesions of the brain; second, those that act indirectly upon the body through the medium of the mind, as intense study over the means of discovering perpetual motion, or even researches into the meaning of certain biblical prophecies.[63] In the ten score pages following this preliminary section, Rush presents what he calls a new nomenclature of mental diseases, from tristimania to manalgia,—a cobweb of technicalities as involved as the Zoönomic classification. Occasionally the author presents clear and illuminating psychological observations, as in his definition of demence as consisting, not of false perceptions, but of an association of unrelated perceptions, wherein the mind may be considered as floating in a balloon, and at the mercy of every object and thought that acts upon it.[64] But in general, Rush in this part of his work has been pronounced often discursive and sometimes inconsequential, with a tendency to expand and multiply rather than to condense and critically classify.[65] The last reference is especially applicable to the earlier articles on the *Different Species of Phobia and Mania.* Among the former are instanced the cat-phobia and the solo-phobia, the phobia being excellently defined as a fear of an imaginary evil, or an undue fear of a real one. Among the latter are described the land-mania which is especially prevalent in the United States; and liberty-mania which shows itself in visionary ideas of liberty and government,—when men expect liberty without law, government without power, sovereignty without a head, and wars without expense.[66]

In these statements the American exhibits all the fanciful ingenuity of the modern French alienists with their movable arrangements of fixed ideas. But he has more solid parts and in his chapter on the derangement of the will is declared to have led his generation and forecasted the later work of Ribot.[67] This estimate seems exaggerated. Rush enumerates but two ways in which the will is affected by diseases, one of which is treated too superficially, and the other too metaphysically. There is first a negative affection, aboulia, or what he would call a debility and torpor, or loss of all sensibility to the stimulus of motives. In this he says he has never been consulted, yet he has been informed by his friend Brissot that animal magnetism will cure light cases. He suggests, however, that persons afflicted with this disorder of the mind should be placed in situations, in which they will be compelled to use their wills, in order to escape some great and pressing evil. A palsy of the limbs has been cured by the cry of fire and a dread of being burned. Why should not a palsy of the will be cured in a similar manner?[68] But to proceed: there is, second, a privative affection of the will, when it acts without a motive, by a kind of involuntary power. Rush is here at pains to set forth the two opinions that have divided philosophers upon the subject of the operations of the will and to grant that freedom is as true as necessity. But in spite of his effort to reach a perfect metaphysical impartiality he finds himself on the necessitarian side of the fence. That derangement of the will in which it acts without a motive, by a kind of involuntary power, is exactly the same thing that occurs when the arm or foot is moved convulsively without an act of the will, or even in spite of it.[69]

Such notions of the diseases of the will as affecting the

[60] Observations, p. 11.
[61] Ibid., Preface, p. vi.
[62] Ibid., p. 16.
[63] Ibid., pp. 30-37.
[64] Observations, p. 257.
[65] C. K. Mills, Benjamin Rush and American Psychiatry, Medico-Legal Journal, Dec., 1886, p. 34.
[66] Columbian Magazine, 1786-7, pp. 110-113, 177-180, 182-187, 305.
[67] Mills, op. cit., p. 10.
[68] Diseases of the Mind, pp. 268-270.
[69] Ibid., p. 263.

moral faculty had at the least a practical value in Rush's ideas of medical jurisprudence; his corresponding notions of the disease affecting the believing faculty has not even a theoretical worth. Assuming a realistic principle of faith he uses it, first, as a peg upon which to hang more anecdotes, then, as a club to throw at the idealists. Defining his favorite faculty as that principle in the mind by which we believe in the evidence of the senses, of reason, and of human testimony, he gives as an instance of its excess an old Revolutionary quidnunc who, like Horace's character of Apella, believed everything he heard; and as an instance of its deficiency Burke's description of those who "believe nothing that they do not see, or hear, or measure with a twelve-inch rule." This incredulity, adds Rush, is not confined to human testimony. It extends to the evidence of reason and of the senses. The followers of Berkeley either felt or affected the last grade of this disorder in the principle of faith. That it is often affected, I infer from persons who deny their belief in the utility of medicine, as practiced by regular-bred physicians, but believe implicitly in quacks.[70] Since it affects both his preaching as a realist and his practice as a materialist, the Scotch-trained doctor now offers a sort of logical prescription for this insanity of doubt. The cure for a weak mental digestion is to go back to a plain intellectual diet,—or as he puts it: the remedy for this palsy of the believing faculty, should consist in proposing propositions of the most simple nature to the mind, and after gaining assent to them, to rise to propositions of a more difficult nature.[71]

In the succeeding chapter on derangement in the memory there is presented a dry catalogue of the various forms of this disease. Lacking a technical nomenclature, it nevertheless contains implicit recognition of the various forms of amnesia. Among those given is an oblivion of names and vocables, of the sound of words but not of the letters which compose them, of the qualities or numbers of the most familiar objects, of events, time, and place. Instances of these lapses in the memory are forthwith presented,—from Rush's own friends to his patients in the Philadelphia hospital,—from the absent-minded Dr. Magaw of the university, to an Italian victim of the yellow fever, who in the beginning of his malady spoke only English, in the middle only French, and on the day of his death only the language of his native country.[72] Rush here obtained an insight into retrogressive amnesia, yet in treating of the results of the weakness and loss of memory he is even more superficial than before. He resorts to the once-rejected scholastic realism, speaking of the objects of knowledge as either sleeping or perishing in the mind. Finally, he gives a most inadequate account of the causes of these things. Among mental causes he mentions the oppressing the memory in early life with words and studies disproportioned to its strength, as prematurely crowding Latin and Greek into boys' minds; and also the undue exercise of memory upon any one subject, as in the case of the negro calculator, Thomas Fuller, of Virginia, who was famous in numbers, but could not recollect faces.[73]

The chapter on dreams and somnambulism is an equally hasty performance, yet may be happily supplemented from other sources. Dreaming is here said to be always induced by irregular or morbid action in the blood-vessels of the brain, hence it is accompanied with the same erroneous train, or the same incoherence of thought which takes place in delirium. This is so much the case that a dream may be considered as a transient paroxysm of delirium, and delirium as a permanent dream.[74] Again, somnambulism is nothing but a higher grade of the same disease. It is a transient paroxysm of madness. Like madness it is accompanied with muscular action, with incoherent or coherent conduct, and with that complete oblivion of both which takes place in the worst grade of madness. Coherence of conduct discovers itself in persons, who are afflicted with it, undertaking or resuming certain habitual exercises or employments. Thus, we read of the scholar resuming his studies, the poet his pen, and the artisan his labors, while under its influence, with their usual industry, taste, and correctness.[75] As a foil to these dogmatic definitions and unqualified assertions, Rush on other occasions made a number of additions and conjectures. Suggesting that dreams are useful to prognosticate incipient diseases and to prevent delirium from too great excitability, he goes on to say that we never dream of things the raw material of which did not exist in the mind previously. So dormant or lost ideas are often revived in dreams and recollected afterwards. The fact that I remembered the name of a forgotten classmate of the Jersey college after a dream proves, not that such a recollection was a preternatural occurrence, but simply that nothing exists in the brain but that which had previously entered through the medium of the senses.[76]

As Rush's sensationalism rescued him from a magical conception of the phenomena of dreaming, so did his materialism from a similar view of the phenomena of somnambulism. Here is given, in a remarkable anticipation of later French discoveries, a case of continuous memory in trances, of patching up recollections into an unbroken secondary series. Somnambulists, he reasons, recollect in each fit what they did in the preceding one, as in the case reported by Dr. Lentwork, [?] of Springfield, to the Reverend Dr. Stiles, of Yale. They appear to have two distinct minds, but may this not be owing to impressions made on the other parts of the brain by diseases and re-excited by the same stimulus?[77] It must be granted that Rush has here ingeniously approached the problem of dual personality, previously ignored, by a sort of anticipated nerve-tract theory.

[70] Diseases of the Mind, pp. 276-7.
[71] Ibid., p. 274.
[72] Ibid., p. 276. Cf. W. B. Carpenter, Principles of Mental Physiology, London, 1879, p. 437.
[73] Diseases of the Mind, pp. 281-2.
[74] Ibid., pp. 300-1.
[75] Ibid., p. 304.
[76] Purnell MS., p. 128.
[77] Ibid., p. 133.

In his next topic he is not so modern. He defines an illusion as a sort of waking dream, a disease in which false perceptions take place in the eyes and ears from a morbid affection of the brain. The deception consists most commonly in hearing our own names, for the reason that we are accustomed to hear them pronounced more frequently than any other words. Hence, that part of the ear which vibrates with the sound of our names moves more promptly, from habit, than any other part of it.[78] This naturalistic explanation is put forward against the beliefs of superstitious people, who say that these false perceptions are premonitions of death. Yet the author is careful to add that it may not be applied to invalidate the accounts of the supernatural voices and objects that were seen or heard by individuals in the Old and New Testaments.[79]

Allowing no conflict between his science and his religion, Rush offers in his final chapter on the *Diseases of the Mind* a plea for what he calls a system of Christian jurisprudence. Though based on a cramped and narrow psychology, it was given a broad and fruitful application. The disease of the will, it is assumed, discovers itself only in the moral faculty and exists with a sound state of the conscience and sense of the deity. Hence, as the lecturer had previously declared, it would be as absurd to inflict the punishment of death upon a fellow creature for taking away a life under a deranged state of the will, as for a surgeon to cut off an arm or a leg because in its convulsive motions it injured a toilet or overset a tea table.[80] Now, while these morbid operations of the will may include in their consequences even theft and murder, yet they are to be considered, not as vices, but as symptoms of a disease. Therefore, for persons thus afflicted legislators should abolish the punishment of death, cropping, branding, and public whipping, and substitute for them confinement, labor, simple diet, cleanliness, and affectionate treatment. As is shown by the moral effects thus produced in the jail of Philadelphia, the reformation of criminals and the prevention of crimes can be better effected by living than by dead examples![81]

This semi-political peroration concludes the last of Rush's philosophizings. Contrasted with the first, the undergraduate transcription of scholasticism, it illustrates his saying that it was time to take science out of the hands of philosophers and put it into the hands of the people.[82] Here is a principle much in the spirit of Franklin. Applied as a criterion to Rush's own works, it shows him to be a popularizer rather than a speculator, an advocate of concrete results rather than of abstract consistency. So, however much Rush accomplished as a practical reformer, the natural and inevitable outcome of such a principle was to make his metaphysics a thing of inconsistencies. As a transitional thinker he strives to be so impartial that he takes both sides at once. His "cold common sense" is offset by a phenomenalism in which "ideas are mere qualities, having no more reality than the sound of a hammer or a bell."[83] So, too, the principle of animal life, excitability, is allowed in one place to be either a quality or a substance;[84] in another it is looked upon as a sort of vital phlogiston, which was to be drawn off from animal matter as freely as Rush himself drew blood from his patients.[85] Again, while diseases of the mind are counted as veritable derangements of a constituted order, real evils in this present world, still it is likewise held that "all evil has wisdom in it, and every folly and vice, like every particle of matter, is necessary."[86]

In fine, if these scattered inconsistencies be fitted into the divisions of epistemology, ontology, and cosmology, Rush's system is found to issue in a mutual cancellation of terms. That this was due to the varying influences of conflicting schools of thought—realism, materialism, and an obsolescent deism—becomes evident in a criticism of his main field of endeavor. Rush's psychology was vitiated by a kind of realistic phrenology, in which imaginary faculties are immured in so many water-tight compartments. Now such a confinement within arbitrary limits had a two-fold defect: it prevented the attainment of a correct view of precise cerebral localization, and of the general activity of the brain in the higher thought processes. Rush is again but half right in his genetic methods. He recognizes the growth of the child mind, and attempts to map out the steps in its mental development; but he fails to see that the decline of the intellectual powers occurs in an order the reverse of that of their acquirement. The doctrine of retrogression, which he touched upon in his mature essay on *Old Age* is twisted by an earlier deistic bias. Giving the order in which the mind declines as first the memory, then the imagination and understanding, he adds, that the sense of the Deity is never forgotten.[87] A lost memory which never forgets something is a cause for astonishment, and yet despite this and his other defects Rush was no more inconsistent than those upon whom he drew. Like the Zoönomic philosopher he put in the same basket fragile innate faculties and lively vital movements. Like Hartley he added teleological trimmings to a doctrine of philosophical necessity: nothing was made in vain; every power, principle, and feeling of the body and mind must answer to the end of their creation.[88] For these things, Rush, as a transitional writer, was hardly to blame. Struggling in the stream of conflicting currents, he was indeed in a poor position to estimate their relative forces. In other words, the times were against him. Historically, he was not so placed as to obtain the right perspective. No more

[78] Diseases of the Mind, p. 307.
[79] Ibid., p. 308.
[80] Medical Jurisprudence, p. 388.
[81] Diseases of the Mind, pp. 365-6.
[82] A. E. B. Woodward, "A System of Universal Science," p. 239, Philadelphia, 1816.
[83] Purnell MS., p. 90.
[84] Animal Life, p. 6.
[85] Cf. Utility of a Knowledge, etc., p. 258.
[86] Purnell MS., p. 90.
[87] Purnell MS., p. 96.
[88] Thoughts, MS., p. 47.

than his masters could be aware of the fact that his realism was a drawing away from his materialism, just as his materialism was from his deism.

Rush's system was a syncretism, a mode in which varied movements were fused. It was, therefore, capable of a variety of interpretations. These it received at the hands of both contemporaries and followers. An anonymous London deist wrote that when it was said that medical men were enemies to the religious view, Dr. Rush was an example to the contrary.[89] So, too, a Philadelphia admirer attributed to Rush the statement that it remains yet to be discovered, whether all the moral, as well as natural attributes of the Deity may not be discovered in the form and economy of the material world.[90] And the same author, in his *Eulogium,* recalling Rush's methods of teaching, said that he urged his students to the study of the anatomy of the human mind, commonly called metaphysics, since the reciprocal influence of the body and mind upon each other can only be ascertained by an accurate knowledge of the faculties of the mind and their various modes of combination and action. To this end they should study Butler, Locke, Reid, Beattie, and Hartley.[91]

Interpreted, then, both as a realist and a deist, Rush was yet in the main a materialist. His followers and imitators at home and abroad show this. His own pupils outdid him in the application of the physical principle. One wrote on the effects of the passions on the body;[92] another on the morbid effects of grief and fear;[93] a third made voluntary motion the effect of irritability;[94] a fourth defined volition as a sensorial power secreted in the substance of the voluntary muscles.[95] These opinions were expressed in the inaugural theses of the doctor's students at Philadelphia. A similar use of his name and opinions is to be found in the theses of the early American students in Edinburg.[96] The contents of these treatises may be as dull as their latinity is indifferent, nevertheless, they are of interest in that while some of them refer to Hartley and Darwin, Franklin and Priestley, all of them refer to Rush and thus go to prove that as head of the Philadelphia school of materialists he was of no small influence. That influence, it should be noted in conclusion, was chiefly exerted in the Southern States. From them came the great majority of Rush's pupils, and if to them be added open-minded thinkers, who, like Jefferson, Cooper, and Buchanan, knew either Rush or his works, the South may be looked upon as the most promising field for the spread of materialism. But why that movement failed to flourish there, and how it was rooted out, is another story, connected with the interplay of conflicting forces. But before taking up the important topic of the decline of the English and French materialistic influences, through the rise of natural realism, or the philosophy of common sense, consideration must be given, for the sake of thoroughness, to the case of the minor materialists.

[89] An Interpretation of the Sacred Scriptures, p. 11, London. 1797.

[90] David Ramsay, Eulogium . . . of David Rittenhouse, p. 27, Philadelphia, 1796.

[91] Eulogium, p. 124.

[92] Henry Rose (Va.), 1794.

[93] William Hall (S. C.), 1812.

[94] John Hart (N. C.), 1806.

[95] Robert Mayo (Va.), 1808.

[96] Such as C. Berkeley (Va.), 1793, De Corpore Humano; R. B. Screben (S. C.), 1799, De Vitae Humanae Gradibus, in the William Osler Collection, in the Medical and Chirurgical Faculty Library, Baltimore.

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A CASE OF MULTIPLE TUMORS IN A DOG.

By Ernest K. Cullen, M. B., Baltimore.

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

Numerous cases of multiple tumors occurring in animals have been reported and the writer merely adds this case to the already long list without any reference to the literature on the subject, because of its interesting feature: the occurrence of two distinct types of carcinoma—squamous cell carcinoma of the skin and adeno-carcinoma of the prostate.

Clinical history.—The dog was a St. Bernard 12 years of age, weighing 180 pounds.

Family history.—The owner states that the dog came of healthy stock and he knows of no history of malignant disease.

Personal history.—The dog always appeared quite healthy until the onset of the present illness.

Present illness.—In the summer of 1900 a small lump was discovered on the dog's back close to the middle line in the dorsal region. This very gradually became larger and at the end of about three years had attained the size of an orange. In February, 1903, the greater portion of the tumor was removed and the base cauterized. Healing was tardy. During the eighteen months following the operation there were no signs of recurrence.

In November, 1904, recurrence was noted at the site of the operation. Growth was rapid and by April, 1905, the tumor had assumed the proportions of a medium-sized cocoanut. A second operation was resorted to and the tumor, together with a portion of the surrounding skin, was removed. The wound healed *per primam* and no evidences of recurrence have since been observed.

Following this operation, however, the dog never regained its former health. It showed signs of a gradually progressive weakness, and during the last few weeks of its life, any attempt to rise from the floor was marked by symptoms of pain. No gastro-intestinal or genito-urinary symptoms were detected. In October, 1905, the dog died rather suddenly.

The autopsy was performed twenty hours after death.

Pathological Report.—The body is that of a large St. Bernard dog. Over both elbows are decubitus ulcers. In the dorsal region of the back, just to the right of the median line, is a linear scar 10 cm. in length. There is no sign of recurrence of the growth in this situation. The axillary and inguinal glands are not enlarged.

On opening the abdomen the spleen is found to be very much enlarged, measuring approximately 30 x 10 x 4 cm. The capsule is tense but the consistence is soft and flabby. On section a considerable quantity of blood exudes from the surface. The picture is one of recent hemorrhage into the splenic pulp. This is rendered still more evident by microscopical examination.

The lungs are œdematous but show no areas of consolidation. The heart, liver, and kidneys, both macroscopically and microscopically, present the usual picture of cloudy swelling. The stomach and intestines appear normal. The bladder shows some injection about the trigone but otherwise appears normal.

Prostate.—The prostate measures about 4.5 cm. in diameter. It is firm in consistence and externally appears uniform. On section, however, definite pathological changes are visible. Surrounding the prostate is a well-defined white capsule measuring 1 to 2 mm. in thickness. Running from this into the substance of the gland are definite bands of stroma (Fig. A) quite similar in appearance. Between these the tissue has a distinctly honey-combed appearance, is greyish-white in color and rather spongy in consistence (Fig. B). In one portion (Fig. C) the tissue is uniform in appearance, with the exception of a few scattered areas, honey-combed in appearance.

Squamous cell carcinoma of the skin.—It is impossible to obtain a gross description of the tumor.

Histological examination.—Scattered in a stroma of loose connective-tissue are numerous irregularly-shaped alveoli. Lining the periphery of these is a row of low cylindrical epithelial cells more or less regular in outline. Internal to this are numerous layers of epithelial cells with oval or spherical nuclei. The cell outlines are indistinct but the predominating cell appears to belong to the basal type. The nuclei vary considerably in size, one nucleus occasionally being three or four times larger than that of the adjacent cell. The majority of the nuclei are deeply stained. Definite epithelial pearls are present in many of the alveoli and keratinization in parts is extensive. The stroma immediately surrounding the alveoli is rich in connective-tissue cells, but the greater portion consists of loose tissue containing a moderate number of small mononuclear cells. Adipose tissue is present in some places.

Adeno-carcinoma of the prostate.—Sections through the central portion of the prostate show the presence of numerous glands with narrow lumina. Many of these have infiltrated the muscle and the picture is distinctly invasive in character. In most instances the glands are lined by a single layer of well-defined cylindrical epithelium. The individual cells are rather uniform in size and shape. The nuclei which are generally situated at the base of the cell are oval or round,

Adeno-Carcinoma of the Prostate (4 Diameters).

The figure represents a cross section of two-thirds of the prostate. Definite bands of connective tissue A are seen passing from the capsule into the substance of the gland. Between these are areas B, which present a distinctly honeycombed appearance. Microscopically these areas show masses of glands undergoing extensive retrogressive changes. At C the tissue looks uniform, but in a few places are seen small areas similar to B.

fairly uniform in size and deeply stained. Nuclear figures have not been observed. A distinctive feature is the occurrence of extensive desquamation and disintegration. Many of the gland lumina are filled with desquamated cells in varying stages of disintegration. In some instances an amorphous débris fills the gland cavity. Only an occasional normal prostatic gland is found and this at the margin of the section, corresponding to the peripheral portion of the prostate. The connective-tissue stroma is rather dense and contains large numbers of diffusely scattered small mononuclear cells.

Remarks.—The uniformity in size of the epithelial cells leads to some difficulty in the diagnosis, but the essentially invasive character of the growth together with the extensive retrogressive changes classes it as malignant.

Examination of the viscera and the various lymphatic glands showed no evidence of tumor metastases.

NOTE.

At the regular meeting of the Second Section of the American Urological Association, held in New York on Wednesday, October 24, 1906. . . . .

The president, Winfield Ayres, M. D., officially announced the death of the vice-president of the Second Section, William K. Otis, and called for a report by the committee appointed for the purpose, to present a memorial on the Association's bereavement. In presenting the report, a member of the committee said:

"The ties of life-long intimacy which bound most of us to Dr. Otis, makes his death a subject of grief to each individual. The usual set form of preamble and resolutions, therefore, were deemed inadequate by your committee to express our sorrow. 'Billy's' demise is, to the older members of the Association as if a much loved brother had gone from us. Your committee begs to submit:

William Kelly Otis' earthly career ended on September 22nd, 1906.

To the members of the American Urological Association, his death is a threefold blow.

Most of us knew him intimately from his childhood; by his decease we lose a consistent friend, a charming companion, a most estimable colleague.

To the Science of Urology his death means an irreparable loss. Cut off in the midst of his career, his inventive genius is stopped; the new and useful instruments he was continually devising must now be perfected by other hands. The advances in our work, he can no longer aid in developing.

The American Urological Association loses one of its founders, one of its most active coadjutors, one of its truest adherents.

Our Association shares with the family of William K. Otis, with the profession at large, and with that world in which true manhood is understood and appreciated, that deep grief which the death of so noble a character inspires."

RAMÓN GUITERAS,
A. ERNEST GALLANT,
FERD. C. VALENTINE, } *Committee.*

NOTES ON NEW BOOKS.

The Practice of Pediatrics in Original Contributions by American and English Authors. Edited by W. L. CARR, A. M., M. D., etc. (*Philadelphia and New York: Lea Brothers & Co., 1906.*)

The Practice of Pediatrics (Carr) is a very well arranged and written work, of 1014 pages. The articles are contributed by 14 pediatric authorities, most of them American, and the whole has been edited by Dr. Walter L. Carr. This work is, on the whole, a very acceptable addition to the present collection of text-books on the subject of pediatrics and is up to date in every department, being strong on treatment, and not having its text overburdened with the discussion of fine pathological points. In regard to the different sections of the work there is little preference to be expressed, each subject being handled in a thoroughly practical manner.

The articles on infant feeding, milk modification and kindred matters, are well worth reading by any one interested in the subject, being not only scientifically correct, but abounding in very practical suggestions on small points that are usually not mentioned, the observance of which, however, might often turn the scale from failure to success in nurture of the baby. Very little knowledge on the part of the reader is taken for granted by the writer, and hence the fulness of his article. The work in general is the conventional text-book, well written by able men, well arranged and indexed. There are not as many illustrations perhaps as some similar works contain, but what there are are satisfactory, exhibiting clearly what they are intended to represent. The colored plates showing the various varieties of stomatis, Koplik's spots and smallpox, are particularly good.

The work is a valuable statement of advanced present day opinions in pediatrics, and will be found helpful to both practitioner and student. H. M. F.

Pulmonary Tuberculosis. Its Modern and Specialized Treatment. ALBERT PHILLIP FRANCINE, A. M., M. D. (*Philadelphia and London: J. B. Lippincott Company, 1906.*)

One must admire the clear, practical, sensible spirit in which Doctor Francine's book is written. Although coming from an enthusiast it is free from undue pretention and exaggeration. The matter is justly considered and plainly put so that it will prove a valuable and safe guide to the large class of physicians anxious to help their tuberculous patients, but deprived of the opportunities of practical and special training. It is agreeably written, the pleasure in reading it being only marred in places by gross typographical errors. There are ten plates in the book, and it seems a pity that where so many instructive illustrations might have been produced, one-fifth of the space should be wasted in showing how to give an injection in the back, and how to apply dry cups. The introductory chapter presents unusually well in such a brief form the modern views on the origin and modes of spread of the disease. The consideration of rest, fresh air, diet, and exercise bears the stamp of a large practical experience with the subject. There are no vague generalizations, the directions being definite and specific. Climate is very conservatively and justly treated. While admitting its value under certain conditions, he emphasizes that it is by no means an essential factor in the treatment of tuberculosis. The home is the place where the largest part of the treatment must be carried out in the greatest number of patients, and in its indiscriminate recommendation, climate has probably totalled more harm than good in the arrest and cure of tuberculosis. To us the chapters on the use of the tuberculins and the specific sera are the least interesting in the book because we miss here the flavor of the author's practical experience and personal judgment. They are, however, good reviews. The use of drugs and the management of complications is very well handled. Although one may not have the confidence the author expresses in certain lines of treatment, his therapeutics are reasonable, and they certainly have the advantages that come from a large experience. Throughout this portion of the book, as well as elsewhere, the importance of secondary infections for an adequate understanding of the cause of the disease and its treatment is emphasized. Their varied manifestations, particularly their rôle in the production of hæmorrhage, are interestingly considered. In the last chapter is told briefly how the whole question of tuberculosis is managed under Doctor Flick's direction at the Phipps Institute. One must admire the remarkable opportunities afforded for study. We gladly agree with the author that opinions coming from the Phipps Institute are worthy of great consideration. L. H.

The Harvey Lectures. Delivered under the Auspices of the Harvey Society of New York, by PROFESSORS HANS MYER, CARL VAN NOORDEN and others. (*Philadelphia and London: J. B. Lippincott Co., 1906.*)

As stated in the preface of this volume, the object of the society "is the diffusion of the medical sciences by means of public lectures. . . . . The lectures are not intended to be merely accounts of experimental work done by the lecturers, except in rare instances. They are rather to be a broad presentation, from the

laboratory point of view, of subjects of general interest. . . . . The lecturers are selected on account of a special adaptation through their own research work in the subjects presented by them." No reader will fail to recognize that in the first volume of these lectures the society has admirably attained its object. Addresses on "Tuberculosis" by Prof. Theobald Smith, on the "Heart-beat" by Prof. Howell, on the "Nerves" by Prof. Barker, on "Trypanosomes" by Prof. Ney, not to mention other papers of equal interest and importance, by men recognized by the world as leaders in their special lines of work, give this volume a distinct mark of individuality and notoriety. To the large lay public, which is taking such an active and intelligent share in the discussion of various medical questions, this volume offers the best and latest information on many topics of general interest; but all medical students also will find the lectures well worth reading and study. If the next volumes of this society's papers are of equal excellence, this society will be more than excused for its birth, in these times when too many societies are created without sufficient reason for their formation. R. N.

International Clinics, Vol. IV, 16th series. (*Philadelphia and London: J. B. Lippincott Co., 1906.*)

This quarterly publication invariably contains a number of valuable and interesting articles, and this volume in no wise falls behind in the excellence of its predecessors. It contains five papers on treatment and an equal number on surgery, six on medicine, three on obstetrics, one each on laryngology and otology. Contributors to this volume are such well-known men as Diculafoy and Bernard of Paris, Grocco of Italy, Squire and Trevelyan of England, and many of equal repute in the United States —Craig of Boston, Porter of St. Louis, Richardson of Washington, Lillienthal of New York, Müller of Philadelphia, etc. Their names are picked at random merely to indicate the interest taken in these clinics both at home and abroad. It would seem invidious to select the subjects of any of the articles for special remarks, but simply to indicate the breadth of these volumes a few titles will suffice: The Prevention and Treatment of Chronic Nephritis, the Treatment of Obesity, Syphilitic Aortitis, Myxœdematous Infantilism and Incomplete Myxœdema, Vesical Tumors, Placenta Prævia and its Treatment. Many of the articles are accompanied by illustrations which add oftentimes to their value, but there is a tendency with authors to overload their papers with photographs or drawings, either reproducing such as have appeared before many times, or introducing others practically identical. Good illustrations can be made so cheaply to-day, that badly colored ones are almost inexcusable, and detract from the pleasure both of articles and volume. Otherwise, the volume as a whole can be commended. R. N.

Studies in Gynecology. By John A. Sampson, M. D. (*Albany, N. Y.: Fort Orange Press, 1907.*)

This illustrates a new method in teaching gynecology. It is essentially a well arranged student's note-book on gynecology, with excellent and numerous drawings by the author and a few stimulating questions relating to and accompanying each drawing. There is ample room for notes by the student himself. There is also an excellent index.

The simple and forceful illustrations, the illuminating questions and the logical arrangement all should make this an excellent aid in acquiring a knowledge of gynecology, and, when completed by the student, should be one of his most valuable reference books.

Mercer's Company Lectures on Recent Advances in the Physiology of Digestion. Ernest H. Starling, M. D., F. R. S. (*Chicago: W. T. Keener & Co., 1906.*)

This work contains so much interesting matter that it is difficult to write an epitome which shall be shorter than the book itself. Nevertheless, an attempt will be made to give some idea of its contents.

Food is required by the organism (Chaps. I and II) for furnishing heat and repairing tissue. For this the food must be completely disintegrated, a condition which is brought about by the action of enzymes. Enzyme action appears to be catylitic in nature. The author favors the view that catalysers have a twofold action (1) by bringing about a concentration of the molecules of the catalyte and (2) by furnishing an intermediary substance which assists in the chemical reaction. That such intermediary bodies are actually formed is made probable by a study of the reaction velocities.

Ferments are reversible in their action. Some scanty evidence indicates that in composition they are probably colloidal in character. The relation of toxin to antitoxin is similar to that of the enzyme and its zymolite (substrate).

In the secretion of saliva (Chap. III) there are no essential differences in the actions of the sympathetic and cranial autonomics Apparent differences are due to variations in vaso-motor actions on the gland. Secretion is a vital process. The cells throw out their secretory products and recoup from the increased blood supply. Some indication of the amount of energy required is found in the increased consumption of oxygen, which is four times as great as under normal conditions. The abstraction of water from the blood may be regarded as osmotic, the pressure being exerted by the split products of cell metabolism.

The lecture on digestion in the stomach (Chap. IV) is based chiefly on the work of Pawlow and his pupils. The experiments of Edkins prove that the second phase of gastric secretion is due to chemical stimuli passing to the gland cells by way of the blood stream and Pawlow was mistaken in attributing this to a local reflex. Thus to variations in the quality and quantity of this chemical stimulus may be attributed the apparent adaptation of the secretion to the requirements of the meal, a view more acceptable than that of the Pawlow school.

In the lecture on pancreatic secretion (Chap. V) after a discussion of the origin and action of secretion the conclusion is reached that it is doubtful whether in the activity of this gland the nervous system plays any part whatever.

Unlike the salivary glands (Chap. VI) the pancreas does but little work in overcoming osmotic pressure and can do but little work against mechanical interference with the outflow from the duct. Here also there is during activity an increased consumption of oxygen. There is histologically no fundamental distinction between the tubule cells and the islands of Langerhans, the latter being merely areas where cell division is taking place. There is nothing to indicate the part of the organ concerned in carbohydrate metabolism.

Enterokinase (Chap. VII) is a true "ferment of ferments" not merely a complement in Ehrlich's meaning of the word. There is no evidence that the character of the pancreatic secretion is adapted to the particular sort of food eaten.

The secretion of the bile (Chap. VIII) parallels that of the pancreatic juice and is produced by the same agency, namely, the action of secretin.

The secretion of the intestinal glands (Chap. IX) may be accelerated by mechanical means or by chemical hormones. One hormone is the secretin which also causes the secretion of bile and of pancreatic juice; the second hormone is the intestinal juice itself which causes increased production of succus, but has no action on the pancreas. The ferments of the intestinal juice are then discussed.

The picture presented by the movements of the alimentary tract (Chap. X) is essentially a combination of the results of Cannon's skiagraphic observations and those obtained at University College by other methods (enterographic, etc.) An essential feature of peristalsis is the inhibition which precedes contraction.

The style is clear, simple and forcible and compares favorably with Pawlow's classic on the same subject.

PERCY M. DAWSON.

Cleft Palate and Hare Lip. By W. ARBUTHNOT LANE, M. S., F. A. C. S. (*London: The Medical Publishing Company, Limited, 1906.*)

This monograph of 60 pages is a résume of various papers written by the author from time to time.

The greater part is devoted to a study of the factors that influence the growth of the naso-pharynx and the mouth, and of the bones that surround these cavities. He considers this most important, since the success which attends operations for cleft palate, so far as perfection of speech is concerned varies directly with the degree of development of the naso-pharynx, and with the freedom of the passage of air through it.

The author believes it very essential to separate the mouth from the nose as early in life as possible, and thinks operations for cleft palate should be done either the day after birth or very soon afterwards.

Lane's method, which is well described and illustrated, is quite different from the ordinary method of paring the edges of the cleft and bringing them together.

Textbook of Comparative General Pathology. By PROF. DR. TH. KITT. Translated by DR. WM. CADBURY and edited by DR. A. J. SMITH. (*Chicago: K. T. Keener & Co., 1906.*)

The general principles of pathology, to a consideration of which this book is devoted, have been worked out very largely by a study of the diseases and experimentally produced disturbances in animals and the similar conditions in man, usually of more vital interest to us, have frequently been cleared up in this way. It is not surprising, therefore, to find that Prof. Kitt's discussion of these general principles brings forward the names familiar to the student of human pathology, and, indeed, it is only the use of certain terms current among veterinarians and the constant references to cows and dogs that reminds one that the book is intended rather for veterinarians than for medical students.

The whole treatment of the subject, as might be expected from Prof. Kitt, is entirely rational and conservative and in accord with the best modern views. Dr. Smith's additions and notes give the essentials of the recent American contributions.

The book deals with the general relations of disease, predisposition and immunity, the causes, course and termination of disease; then with circulatory and metabolic disturbances, inflammation and repair, tumors and functional disturbances. All of these are treated broadly with illustrations and references to the diseases of domestic animals which are more specifically described in Prof. Kitt's Special Pathology. It is well translated, illustrated, and printed, and aside from its primary value to veterinarians, it may be highly recommended as a text-book of general pathology to other students of medicine.

Pathogenic Micro-Organisms, Including Bacteria and Protozoa. By WILLIAM HALLOCK PARK, M. D. (*New York and Philadelphia: Lea Brothers & Co., 1905.*)

The second edition of Dr. Park's Manual of Bacteriology has been very extensively enlarged and improved, and, in its present form, can be most cordially recommended, not only to students of bacteriology, but to advanced workers and practicing physicians. In preparing it, Dr. Park has taken advantage of his exceptional experience in public health work gained through several years' association with the Board of Health in New York City, and on this account the chapters on diphtheria and tuberculosis are extremely valuable, especially from the diagnostic standpoint. In addition to the vast amount of practical information contained in the book, Dr. Park has taken up in a very pleasing way the consideration of toxins and antitoxins and their mutual relationship. The sections devoted to this phase of the subject are not rendered obscure by the presentation of complicated formulas and diagrams, and are, we think, far more readily understood by the average student than the prevailing expositions in other textbooks. This clearness may be possibly due to the author's facility in expressing himself in excellent English or may result from his knowledge of the subject gained from research work and not purely from the literature. Too much space is not given Ehrlich's well-known theories, while careful attention is devoted to the observations of Nuttall, Wassermann, Metschnikow, Meyer & Ransom, Wright, and Neufeld.

Part III is given up to a consideration of protozoa by Dr. Anna W. Williams and Mr. L. B. Goldborn. While one may doubt the wisdom of including in a manual of bacteriology such a broad subject as protozoa, no one could possibly criticise the way in which the material is presented. Furthermore, a textbook dealing so largely with the subject of vaccination and serum-therapy would not be complete without a consideration of rabies and small-pox, and the authors have clearly justified themselves in their plan of treating bacteria and protozoa in the same volume. The section dealing with rabies is especially well written and bears the impress of coming first-hand from an authority on the subject.

One or two special points in regard to minor details in the book may be mentioned. No satisfactory description of *Bacillus ærogenes capsulatus* is given, the few paragraphs on page 380 being quite inadequate, when one considers the wide distribution of the bacillus and its great pathogenic importance. The *Bacillus icteroides* still finds a place in the list of pathogenic micro-organisms, although its relation to yellow fever can no longer be held even remotely possible.

In the section devoted to the bacteriological examination of water, in considering the isolation of the typhoid bacillus from this source, Dr. Park has not placed sufficient importance, we think, upon the few cases in which the organism has been obtained and identified by all the tests known to bacteriologists. Unless one admits the possibility of the typhoid bacillus surviving a considerable time in water, the etiology of enteric fever remains very obscure, and the rôle of infected water in spreading the disease correspondingly problematical. We now have a considerable number of cases on record in which *Bacillus typhosus* has been obtained from water and identified by its cultural reactions, its agglutination, and by the Pfeiffer phenomenon. Such observations, we take it, are of very great importance, and failure to include them renders the epidemiology of typhoid fever difficult to understand.

Lastly in the treatment of rabies by cauterization, Dr. Williams calls attention to the very great value of this measure in preventing the development of the disease and in ameliorating the severity of the attack, especially if the cauterization be carried out within a short time after the infliction of the wound. Furthermore, its value, even after the lapse of 24 hours, has not been disproved by experimental evidence. Since this practice has largely fallen into disuse or even disrepute, it is a matter of importance that its beneficial results should be properly estimated.

W. W. F.

Progressive Medicine: A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HOWE, M. D., etc.; and M. R. U. LANDIS, M. D., etc. (*Philadelphia and New York: Lea Brothers & Co., Vol. IV, December, 1906.*)

This volume contains five reports on (1) disease of the digestive tract and allied organs, the liver, pancreas, and peritoneum; (2) genito-urinary diseases; (3) diseases of the kidneys; (4) anæsthetics, fractures, dislocations, amputations, surgery of the extremities and orthopedics; (5) practical therapeutic referendum,—all well treated by men recognized in the profession for their special knowledge in the subjects they discuss. For doctors

who have no good medical library of current journals to refer to, or who are too occupied in practice to read the literature of the branch of medicine or surgery in which they are most interested, this quarterly digest must prove itself of real value. Here in a volume of medium size, well printed, and with a good index, a busy practitioner can in a short time easily see the advances and changes which are constantly taking place in the knowledge and treatment of diseases, and so can keep abreast of the latest work done along all the lines of medicine and surgery. For the laboratory student, also, the book is useful, as he, too, can readily find in the volume reference to the more important articles, on which the reports are based. R. N.

A Treatise on the Motor Apparatus of the Eyes. By GEORGE T. STEVENS, M. D., PH. D. (*Philadelphia: F. A. Davis Company, 1906.*)

A perusal of this work unavoidably suggests the question: Are ophthalmologists the world over, so far as the muscular anomalies of the eyes are concerned, groping blindly in the dark, prescribing prismatic and other lenses for faults which are wholly unreal, and performing tenotomies for conditions which exist only in their imagination, or is the author a hobby rider of "monumental" proportions?

If, in most instances, the several varieties of heterophoria and all forms of non-paralytic squint are really, as the author tells us (pp. 261, 417, 418) caused by "declinations" (of which, it seems, there are two types, "normal" or "anomalous" (sic) declination and pathological declinations, p. 236) acting in conjunction with a departure from a condition which he denominates "euthyphoria" (of which, again, there are four kinds, anophoria, kataphoria, anotropia and katotropia) then, indeed, are ophthalmologists in general profoundly ignorant of the whole subject of what has been termed ophthalmic myology. But, on the other hand, if all this ex cathedra teaching of Dr. Steven's is but the outcome of, let us say, a psychic heterophoria on his part—and we cannot deny a strong bias in favor of this view—then the outlook is not so dark, and the ophthalmological world may breathe freely again and not wholly lose heart.

In considering how much weight should be given to these novel, not to say revolutionary views, it seems pertinent to inquire: Has the author established such a reputation as a pioneer in ophthalmological teaching as to lend import to whatever doctrines he may advance? Are his views in other directions, ophthalmological, sound, and his arguments in support of them logical and convincing?

The extravagance of the claims put forth in his "Functional Nervous Diseases" (1887) as to his success in curing epilepsy by operative and other treatment of the eyes, is a sufficient answer to the first inquiry.

The answer, in a negative sense, to the second inquiry is not far to seek. If there is one well-established fact in physiological optics, it is the close relationship which exists between "accommodation" and "convergence," between the conjoint action of the internal recti muscles in converging the optic axes and the action of the ciliary muscles in focusing the eyes for the sharp seeing of near objects. This intimate relationship, because it does not harmonize with his peculiar views regarding the etiology of squint, Dr. Stevens denies, and, fortunately for our purpose, he sets forth, on page 398, the grounds upon which he bases this denial. Let anyone familiar with the subject read this page, and he can reach but one conclusion as to the author's capacity for logical reasoning. In the extremely improbable case that he should ask for further evidence before coming to such a definite conclusion, let him read, on the two succeeding pages and on page 256, what is said as to the action of convex glasses in controlling convergent squint—that it is through their accidental prismatic effect, and not at all through lessening accommodative tension, that they accomplish this result.

We have spoken of the author's shortcoming as a pioneer investigator and as a logical reasoner. The amazing data, opposed as they are to the experience of all other observers, given in the "Table of elements in strabismus" (pp. 409 *et seq.*) would seem to indicate that he has one other noteworthy shortcoming—a lack of capacity for accurately observing and recording scientific facts.

In this table, which purports to give the state of refraction of the eyes in two hundred consecutive cases of non-paralytic squint, met with in private practice, it is set down that 74 (32%) of these 200 strabismic individuals were emmetropic (!). That is to say, the percentage of emmetropia was approximately twice as great as it is in normal-seeing, non-asthenopic individuals taken at random in any civilized community. Again, we find it recorded that of the 84 cases of divergent squint 23 only were associated with myopia, while 38 were associated with hypermetropia and 23 with emmetropia. And, again, that of the 67 cases of convergent squint hypermetropia was present in only 20, while emmetropia was present 29 times and myopia 18 times. These figures, well, if "astounding" is a stronger word than "amazing," we certainly should have used it in characterizing them.

In endeavoring to magnify the importance of his own contributions to the subject of heterophoria, the author tries to make it appear that previous to his publications on the subject little or no account was taken of the state of the muscle-balance except at the reading distance,[1] and that the tests employed had reference only to insufficiency of the recti interni. In this connection, he refers to the section on "Muscular Asthenopia" in Soelberg Wells "Diseases of the Eye," and remarks: "His tests for the affection were made at the near point." (p. 18). Had he read the whole of the section to which he refers, he would not have fallen into this error; for, after describing the vertical diplopia test as made at the reading distance, Wells goes on to say: "We must next test the degree of disturbance in the lateral equilibrium a little further off, and finally at a distance, a lighted candle forming the best object."[2] He would have found, moreover, on the preceding page this statement: "But if either the *internal* (italics our own) or external rectus considerably exceeds the normal standard of strength, the double images will not only show a difference in height, but also a lateral difference."

We were disposed to take exception to what is said (p. 333) as to the slight value of prisms in the treatment of heterophoria; but we hesitate to do so after noting that the author's statement upon this subject "is made from an experience doubtless greater than has been presented to any other observer, and is made without reservation." The air of complacence manifested in this assertion, it may be remarked, obtrudes itself upon the reader, from, preface to index, with what, in the expressive language of Falstaff, might be termed "damnable iteration."

The statement (p. 450) that in the author's opinion word blindness "should be classed among the affections of the eye muscles" needs no comment.

Among the minor faults noticed in glancing over the pages of this book—besides such evidences of careless proof-reading as "Stratfield" for "Streatfeild" (pp. 407 and 496), and "Annals c'Oculistique" (first page of preface) for "Annales d'Oculistique," the "c'Oculistique" being corrected in the Errata, but not the misspelling of Annales—may be mentioned the reference (p. 329) to chloral and sulphonal as coal-tar preparations, and the statement (p. 454) that "in paralysis of an external rectus the

[1] Thirteen years before the appearance of Stevens' "Functional Nervous Diseases" the reviewer published in the American Journal of the Medical Sciences, Jan., 1874 (Vol. LXVII, p. 65), a paper, in which mention is made of tests of the muscle-balance for distant as well as for near vision; and even then it would have been absurd to speak of these tests (the well-known vertical diplopia tests of von Graefe) as novel.

[2] Diseases of the Eye, Henry C. Lea's Son & Co., 1883, p. 721.

head turns toward the side of the unaffected muscle," exactly the reverse of this being what actually happens.

Ophthalmology, unquestionably, is indebted to Dr. Stevens for introducing a very convenient terminology for the latent muscular anomalies of the eyes[3] and, less conspicuously, for directing attention to the significance of these anomalies, and were he content with this measure of credit the critic would be niggardly who denied it him. But, when he goes further and claims (pp. 19 and 20) that the conditions to which he gave these new names were previously unrecognized, he need not expect even a generous critic to concede the rightfulness of his claim, nor be surprised if the critic who is simply just should insist that in general what is new in his teachings, apart from his terminology, is but half true, and that what is true is far from new. S. T.

Chemistry: General, Medical, and Pharmaceutical, Including the Chemistry of the U. S. Pharmacopœia. A Manual on the Science of Chemistry and its Applications in Medicine and Pharmacy. By JOHN ATTFIELD, F. R. S., M. A., PH. D., F. I. C., F. C. S., Lecturer on Chemistry in the University of Edinburgh, etc. Nineteenth Edition. pp. 756. (*Philadelphia and New York: Lea Brothers & Co., 1906.*)

The first edition of this work appeared in 1867. Since that time there have appeared nineteen editions. This alone is sufficient testimony that the book has been a very useful one. The question which presents itself here is whether the work is a suitable textbook for the medical student of to-day. The whole subject of chemistry has made enormous strides since the earlier editions of this book appeared and demands correspondingly greater consideration in medical training.

The book includes a consideration of the following topics: Principles of Chemical Philosophy, Inorganic Chemistry, Organic Chemistry, Physiological Chemistry, Chemical Toxicology, Clinical and Microscopical Examination of Morbid Urine. In addition to this the concluding sections form a laboratory guide of Quantitative Analysis.

It is hardly necessary to state that the book is entirely inadequate for the medical student of to-day, as the mere enumeration of the subjects considered in this small volume is sufficient to establish the fact.

All of these branches require works by specialists in these subjects as medical education has advanced far beyond the point where this sort of book embracing the entire range of chemistry is desirable. The subject-matter is often so condensed as to be utterly beyond the grasp of any student depending entirely upon this book. It is far better suited for students of pharmacy than medicine. A. S. L.

A Textbook of Human Physiology. By DR. ROBERT TIGERSTEDT. Translated from third German Edition and Edited by JOHN R. MURLIN, A. M., PH. D., with an introduction by PROF. GRAHAM LUSK, PH. D., F. R. S. (*New York and London: Appleton & Co., 1906.*)

This work is attractively printed and bound in one volume, comprising 751 pages. It is the translation of the third edition of the well-known two-volume "Lehrbuch der Physiologie des Menschen" of Prof. Tigerstedt, which has enjoyed unusual popularity in Germany as a textbook for students of physiology since the publication of the first edition in 1897. The third German edition appeared in 1905. The translation is abridged, and, as stated by the translator in the preface, especially certain mathematical considerations concerning circulation and vision have been omitted, the idea being to bring the work within the reach of the second year medical student of this country.

Rather unusual in a book of this scope are the first two chapters, the former concerned with graphic methods, the latter with the general physiology of the cell. The former should be very useful to a student's first introduction to physiology, giving a fundamental conception as to by what means results are obtained and assisting him in the interpretation of physiological tracings. The second chapter has its usefulness for those students entering upon a study of medicine without previous biological training. It is with much regret that we realize that this chapter indeed has its place.

All those who are familiar with the writings of Prof. Tigerstedt are impressed above all with the conciseness and ease with which an effort is made to make each subject a unit, and, in so far as possible, complete. In an effort to abridge in certain parts of the translation, this important characteristic has been lost. The chapter upon vision suffers most in this respect. A fundamental understanding of the physical principals involved is necessary for the subject of vision, and if a student is unable to understand this, he will be unable to gain a proper conception of the subject itself. It is, however, not alone the physical and mathematical portion in vision that suffers at the hands of the translator. The result is an impression of discontinuity; rather a series of notes upon the subject than a connected account. This criticism applies to a somewhat less extent to the chapters upon circulation.

There are certain notable exceptions to this; especially the chapters upon the central nervous system, metabolism and nutrition. These are excellent for the purpose they are supposed to fulfill.

A few important references are given at the end of each chapter. In the reviewer's opinion, this is not so useful as references to certain articles of fundamental importance in the text.

Aside from these criticisms, the translator has performed his task well. The English is excellent, the proof corrections carefully done, and there is no trace of the original German.

J. A. E. EYSTER.

Mediterranean Fever in India: Isolation of the Micrococcus Melitensis. By CAPTAIN GEORGE LAMB, M. D., I. M. S., and ASSISTANT SURGEON M. KESAVA PAI, M. B., C. M., Madras. New Series. No. 22. Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. (*Calcutta: Office of the Superintendent of Government Printing, India, 1906.*)

The writers report in detail 17 cases of Mediterranean fever which were studied carefully in regard to their specific agglutinating reaction with M. melitensis as described by Wright.

In many cases a definite diagnosis was obtained only by means of this reaction which is believed by them to be specific.

The results of other workers are reviewed in some detail. Numerous control experiments were made on natives of India, many of whom were undergoing inoculation against rabies, and no agglutination was obtained except in one case. This case one year previously had had a very suspicious fever of remittent type.

Of the entire 17 cases, 11 showed M. melitensis in cultures obtained by splenic puncture. The cultural characteristics of M. melitensis are described at some length.

The organisms obtained from the first two cases were used to inoculate monkeys who took the disease and ran a fairly typical course. The organism was isolated from their blood at various times and from the spleen and liver of one after death.

The smaller group of six cases gave a good agglutination with M. melitensis which was considered sufficient in the light of the preceding cases. The grade of dilution which was followed by a definite agglutination varies quite widely, from 1 to 40 in some to 1-1200 in other cases.

The organism was isolated from the spleen in all stages of the disease—usually in the acute febrile period. One case showed a

[3] The new names which he proposed for the manifest muscular anomalies—the several varieties of squint—have not been, and are not likely to be generally adopted.

mild relapse after a period of six months' freedom from symptoms. One attack seems from clinical evidence to confer an immunity for a long space of time.

In a foot-note mention is made of 19 additional cases from one of which the M. melitensis was isolated by splenic puncture. Many of the cases occurred in groups, forming definite epidemics but no conclusion is reached concerning the method of spread of the infectious organism. They conclude that Mediterranean fever is both common and widespread in India. Temperature charts of the individual case are appended. G. H. W.

The Anatomy and Histology of Ticks. By CAPTAIN S. R. CHRISTOPHERS, M. B., I. M. S. New Series. No. 23. Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. (*Calcutta: Office of the Superintendent of Government Printing, India, 1906.*)

The writer calls attention to the importance of ticks as carriers of disease in some of the cattle fevers, relapsing fever in man and other unclassified "tick fevers" or spirilloses. He considers a careful anatomical description of two species to be all that is required for a clear understanding of all the known species which closely resemble one of the two examples: 1. Rhipisepholus annulatus; 2. Hyalomina ægyptium.

Pyroplasmosis in cattle, dogs, sheep, horses are transmitted by ticks and the same cycle holds for all. The female bites an infected animal and only adults of the second generation are infectious; the female dies immediately after laying her eggs, numbering from 100 to 10,000, according to the species.

The habits of the various ticks are described with care and vary greatly in different species. Their external anatomy has been carefully described by many writers, and this chapter is quite short, but he gives a careful description of the technique which he found useful in its study.

Internal Structure of Ticks.—This makes up the main bulk of the article, and the writer goes into considerable detail, which is justified by the fact that he could find no comprehensive work on this subject. His gross descriptions are much more complete and satisfactory than the microscopic ones. The process of digestion of the blood in the tick's alimentary canal is described microscopically and shown to be as a rule incomplete. Ticks examined months after a meal showed the presence of a black granular detritus in the diverticula of the alimentary tract and such residue is never passed into the rectum. The rectum is connected with the malpighian tubules and serves solely as their excretory receptacle.

The embryology of ticks occupies only a short chapter and one fact is emphasized, namely, that the yolk of the ovum becomes the system of alimentary sacs in the adult. It is shown that the alimentary sacs of the nymph of Ornithodorus contain the remains of the yolk of the ovum.

The plates are numerous and clearly drawn, but the lettering of many is faulty. G. H. W.

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ON THE LIBRARY OF A MEDICAL SCHOOL.[1]

By William Osler, M. D.

One day last spring a London bookseller called and said he had a library of seventeenth and eighteenth century medical books for sale, which had been gathered by the physicians connected with the Warrington Dispensary. Looking over the catalogue I saw at once that it was a collection of value, and knowing that it would supplement very nicely the special libraries which have gradually grown up in connection with the Johns Hopkins Medical School, I wrote to Mr. W. A. Marburg and he authorized me to purchase it and to have it put in good order, and this has been done, and to complete his generous gift, Mr. Marburg has furnished bookcases as well. Dr. Welch will speak of some of the special works. I may mention in passing that the library is very rich in English medical pamphlets of the seventeenth and eighteenth centuries, and contains a large number of the works of classical medical authors which we had not in the library.

A word or two on Warrington and the men who collected these books: This old town on the banks of the Mersey, partly in Chester, partly in Lancashire, had in the middle and latter part of the eighteenth century a notable group of scientific and professional men. The Aiken family made the place celebrated as a literary center, as it was largely through the Rev. John Aiken that the Warrington Academy became so famous. His son John became well known through his "Biographical Memoirs of Medicine in Great Britain," and the large work on "General Biography." A sister of the elder Aiken was the distinguished authoress, Mrs. Barbauld, and Lucy Aiken, a daughter of Dr. John, became a well-known figure in English literature. But by far the most important of the scientific men who lived here in the eighteenth century was Joseph Priestly, who was tutored in "classics and polite literature" at the academy for six years, from 1761. He must have had a very stimulating effect on his colleagues. A very notable character who also has a strong interest for us on this side of the water is Thomas Percival, who was born at Warrington and practiced there before going to Manchester. Upon his work, "Medical Ethics, 1803," was founded the code of ethics of the American Medical Association. I see it stated that a brother of this Percival was also a well-known physician at Warrington, and at his death left a very large library; some of the books may possibly be those before us this evening. James Kendrick was a physician and naturalist of the same type. It was by the exertions of these men and their colleagues that this library was formed. The influence of the Warrington Academy, the educational college of the Unitarians of England, made the town a literary and scientific center, and the medi-

[1] Remarks made on the occasion of the presentation of the Marburg collection of books to the Johns Hopkins Medical School, January 2, 1907.

cal profession must have benefited largely from the intellectual environment of the place. So prominent indeed did it become that a Press was organized, and in looking over Miss Nutting's interesting collection of books on "Nursing," to which I shall refer later, I noticed that from it the works of the celebrated philanthropist, John Howard, were issued. Altogether, the collection has an affiliation with a remarkable group of men, and its value is not a little enhanced to know that it has been used by such men as Priestly, and John Aiken, and Thomas Percival.

The occasion offers an opportunity to make a few remarks upon the future of the libraries connected with this school.

Books are the tools of the mind, and in a community of progressive scholars the literature of the world in the different departments of knowledge must be represented. With the existing arrangements we have gradually built up two libraries, one connected with the hospital and the other with the university. In the former are to be found the modern works and journals relating to medicine, surgery, obstetrics, and the various specialties. Under Dr. Hurd's fostering care this side of the library has grown rapidly, and we have had several valuable donations from the libraries of the late Dr. Donaldson and the late Dr. Chatard. Files of all the more important medical journals are there to be found, and we can all testify to the very stimulating influence which this library had had upon the hospital staff and upon the senior medical students.

After the medical school had opened and the laboratories of anatomy, physiology and pharmacology been erected, the University began the collection which is in this building and which represents the modern works and journals in those scientific subjects upon which medicine is based. There are now very complete files of the scientific journals of anatomy, embryology, physiology, pharmacology, and physiological chemistry. While, in some ways, the ideal plan is to have a special library of each subject in each laboratory, the buildings here are so close together that it was thought best to concentrate all of the collections in this building.

Now it is along these two lines that a library of a medical school should progress, but there are one or two other sides of the question which may be considered. In a large city with another active medical library supported by the profession, the two should work in harmony, as great economies could be effected, particularly in the purchase of the more expensive works and journals. I am glad to know that the library of the Medical and Chirurgical Society is prepared to co-operate with the other medical libraries in this city in some such plan. It is not worth while for the library of the medical school to deal extensively with local literature or with the transactions of the State societies, or to attempt to keep files of all the smaller American journals. There are two other directions in which the library of a medical school should grow, and they are well represented by the collections presented to-night. When a man devotes his life to some particular branch of study and accumulates, year by year, a more or less complete literature, it is very sad after his death to have such a library come under the hammer—almost the inevitable fate. Fortunately, such libraries are very often offered for sale *en bloc,* and this was the case with the large collection of works on teratology and embryology formed by the late Professor Ahlfeld, of Germany. Through the liberality of Mr. W. F. Jencks this very valuable library has been secured for us and will be presented to-night by Dr. Williams. These special groups of books are of the greatest value to the student. It is interesting to know that in connection with the training school of the hospital Miss Nutting has gradually formed a library of all the works relating to nursing and to the care of the sick in peace and war, and I may remind you that we are already the fortunate possessors of another remarkable collection, that of the late Dr. Fisher, who gathered together the set of portraits which was presented to the hospital a few years ago by Dr. Kelly.

This Warrington collection represents a fourth side of the library work. I think you will all agree with me that the interest which has been taken here in the history of medicine and in the biography of the great men of our profession has had a very stimulating influence on the younger men, in giving to them that historical outlook so important in scientific research. The library of a great medical school should contain the original works of all the great masters of medicine. No book should be added to a library simply on account of its age. As in modern literature so in that of the sixteenth, seventeenth, and eighteenth centuries, there is an enormous quantity of trash which is hardly worth shelf room. I would have *all* of the original works of *all* of the great men; and one special value of this Marburg gift is that it is so rich in original editions of many of our masters. For example, I would have in such a library a carefully selected group of the works of Hippocrates, not everything, of course, but the standard editions, such as the Aldine folio, and the editions Frobenius and the more important translations; the editio princeps of Celsus, 1479; the more important of the works of Galen, including the fine Aldine edition, 1525; good editions of Dioscorides, Aretaeus, and of Pliny, and of the other great medical writers of the Greco-Roman school. On the same principle should be collected the chief works of the Arabian physicians, and a shelf or two should be devoted to the school of Salernum. The great medical Humanists should be well represented—Linacre, Caius, and others. Every scrap of the writing of such a man as Vesalius should be collected. A good beginning has been made with the 1543 edition of the "Fabrica," but of such a man all the editions of all his works should be here. The same may be said of such great anatomists as Fabricius, Malpighi, Eustachius, Sylvius, and many others of the sixteenth century. The original works of the great physiologists should be sought for. Every scrap of the writings of Harvey (and they are not numerous) and every edition should be here. In practical illustration of my remarks I beg to present to the Marburg collection an

original edition of the "De Motu Cordis," 1628, perhaps the greatest single contribution to medicine ever made, and which did as much for physiology as the "Fabrica" of Vesalius did for anatomy. The "De Motu Cordis" has become an excessively rare book. I had been on the outlook for a copy for nearly ten years. It had not appeared in an auction catalogue since 1895. Then in August of last year a very much cut, stained and unbound copy was offered to me at a very high figure. It had come from the library of Dr. Pettigrew, the author of a work on "Medical Biography." I had been waiting a long time for a copy, but this looked so shabby and dirty that I decided not to take it. Some months later the booksellers sent the copy back nicely cleansed and beautifully bound, and this time I succumbed. Within forty-eight hours the same dealers sent me another copy from the library of the late Professor Milne Edwards, of Paris, uncut and very nicely bound, which they offered at the same price. Naturally, I took the larger copy and the other one went to a friend in this country. The copy I here present to the library has been a little too energetically cleansed, so that the leaves are very tender and in places have had to be repaired. It came from the library of a physician in London and the bibliographical data are found attached.

I would have the complete works of the Hunters, every fragment available of John Hunter's; everything of Haller—and that means a great deal—of Majendie, and a complete collection of the monographs of great modern physiologists, such as Claude Bernard. The original works of the great clinicians, of Boerhaave, Morgagni, Bichat, Laennec, Louis, Corvisart, Bright, and Addison should be on our shelves; and lastly the great works relating to the history of medicine and to medical bibliography should be collected. Books in the special historical and bibliographical department of the library could very well be added to this Warrington collection, in which way the university could express its appreciation and gratitude for the very generous gift received from Mr. Marburg.

And one word in conclusion—when the plans for the medical school were under discussion, I drew in outline what I should have liked to see on this plot of land. Very much idealized it would have taken many millions for its realization. Surrounding the entire square ran beautiful stone cloisters (ornamented with busts and statues of the great men of the profession), and uniting the four chief buildings which stood in the middle of the sides of the square. On the Monument Street front was a beautiful structure in stone devoted to the library and museum. This part of my plan could yet be realized. As the museum collections grow, and as year by year the books increase in number such a building will become a necessity, and in it these special libraries will find their appropriate home.

SOME ANA OF THE MARBURG COLLECTION.

By M. L. Raney,

Assistant Librarian of the Johns Hopkins University.

In the present paper no attempt will be made to stand upon other than native, or rather invaded, ground. Neither a physician nor the son of a physician, with a view of the science even in broad outlines as yet foreshortened, it would be effrontery in me to appraise this collection as documents in the history of medicine. Nor would it be very edifying to abstract a premier on the subject and of the titles mentioned underscore those which we now possess. As Dr. Cushing kindly suggested, in extending this invitation, there are many interesting details concerning them as books, regardless of their medical contents.

I am asked to appear in the role of bibliographer, a part, be it quickly agreed, entirely too large for a young head, since it can be acquired only by long years of cumulated detail, and yet one to which I could not confine my interest. The bibliographer is said to write about books, treating of their authorship, printing, publication, etc. This is to be an intellectual mechanic. The librarian cannot be thus occupied wholly. He may exercise himself in bibliography, but if his higher powers would not suffer atrophy, he must be ill-contented to limit his attention to these carriages of human thought, as to any other mere trappings of greatness. The busying of one's self exclusively with the externals of a volume has no appeal for me. As chest-weight and dumb-bells in the spare hour it is worth employment, but the metamorphosis into a walking catalogue is mental pugilism. Of the great divisions of human thought it is his professional duty to keep his knowledge bright, not to mention a thorough acquaintance with library economy, which will occupy the bulk of his official hours, and without which he is a luxury incalculably expensive to his institution. The librarian who guards but cannot unlock his treasures is a survival of the Middle Ages. The master results under great rubrics he, as any intellectual man, should have in mind as a part of his working force. But the small labor, in minute divisions, with all its temporary scaffolding of intricate technology, he may pass over, and await the stroke of genius that brushes aside processes, brings unity out of detail, and fixes one more clear truth in the record of our race. The large accomplishment in all extensive fields should be a part of the fiber of him, and professionally he should be able to perform the mechanical service of pointing out the fields where important work is building. Of

those who have wrought and taught highly, therefore, he may not be satisfied to know the street address in the centuries, and the personal inventory, but have right to knock at the door and find welcome. And yet but little more esteem should be accorded a bibliolater than to any other fawning worshiper of stock or stone. A certain interest does attach to any relic of the centuries, though the book be only a paltry one; just as also to a mummy, which may have been an Egyptian numbskull. It is a noble feeling, however, which prompts one to keep about him the *imagines* of those who have pushed the boundary farther and helped put into our hands the sceptre we hold. They may be grizzly; their frock may not please the trim publishing tailor of the present. But there were princely fashions in many of those days, and even if this could be denied, is it not the true spirit which wishes to see them as they saw themselves? With, therefore, no feeling of the interloper or the coachman I indulge in some ana of this catalogue. And let it be added that this phrase is used advisedly; for if our list of books did not contain great names, it could not rightly demand time of us to detail its words and ways. The fact that we have here the text of many who have made history in medicine must ever constitute its chief interest. But it remains true that these messengers, with their precious script from kingly minds of other days, have had, many of them, an eventful journey hither to our abode. It is a very few of these stories that I would recount—few, since the more inexperienced of us had better be made sure of these than have a mere register of a multitude.

These books are old, we all know. They have come a long way. But how long, and what does this signify? In noting the chronology of these publications, as of all books remarked for their age, we must take caution against kindling enthusiasm too early. In most instances, books are not so old as they seem; and old ones are not all rare. There are many other causes of rarity besides age. It is decidedly more difficult to get first editions of Tennyson's early writings, for example, than a host of books four centuries old. The productions of the infant press, incunabula, cradle-books are in large part rare. Those in the first quarter of a century, *i. e.*, up to about 1480, very rare. These have come from afar. But very few printed since 1650 derive any special value from their age. Books, which are sought, generally get their enhanced values from scarcity. This may arise in many ways; so that in fixing the commercial status of a volume, no man's opinion is to be taken who has not had much experience in the markets of the world. Some of the other causes, besides the wear and tear of time, contributing to scarcity, may be briefly set down here to get a proper perspective in considering this collection's age.

1. There may not now be many copies because there never were many, *i. e.*, the edition was limited. This is generally true of the early presses of the fifteenth century, though not every volume, as noted above, antedating 1500, is rare; since toward the close of that century the editions were large and reprint frequent. Of the first edition of Livy, Rome (1469), only one copy on vellum was issued. Private presses are usually very sparing. Most of the editions of the Shakespearean and other critical essays of J. O. Halliwell-Phillipps were limited to forty copies or even less. Only last year our University library received from the estate of H. R. Bishop a copy of "Investigations and Studies in Jade," two sumptuous volumes limited to 100 copies. Of many books only five or ten copies were published. Under this rubric may also be mentioned local histories and early Americana. If the issue was large enough, it has often been reduced by mishap, especially fire. A striking instance I shall presently have occasion to cite from our own collection. As late as 1899 the entire edition of J. L. Humfreville's "Twenty Years Among our Savage Indians" perished in a Hartford fire, except two copies deposited for copyright in the Library of Congress.

2. The cost of production, either from the extent of the work, or from its expensive materials, also bars wide circulation. Baron von Humboldt used jocosely to remark that he could not afford to own a copy of his own work.

3. Illustrated works may owe their scarcity not only to the cost of their production, but also to the fame of their illustrators, or to the superiority of the first impression, since this becomes duller with each succeeding issue.

4. The first edition of any work may gather interest from the subsequent fame of the author. I have mentioned Tennyson. Remember, too, his friend Edward Fitzgerald, whose rendering of Omar Khayyám's quatrains, "issued in beggarly disguise as to paper and print, but magnificent vesture of verse," in 250 copies; unpurchased save a fifth of it at the end of eight years; put in despair outside the publisher's door in a box marked "All these a penny each"; discovered, among others, it is said, by Rossetti and Swinburne; and then at auction in 1898 a copy bid in by the publisher himself, Mr. Quaritch, at £21.

5. Many books are rarely procurable owing to the printer's renown. Among famous names in the first two centuries of printing may be mentioned Gutenberg, Fust, and Schoeffer in Germany; Aldus Manutius and Giunta in Italy; Caxton, Wynkyn de Worde, and Lettou in England; Plautin and Elzevir in the Netherlands; Froben in Switzerland; Verard, Badius, Estienne, and Wechel in France. In the next two centuries noteworthy names are Bodoni of Parma, Didot of Paris, and Bulmer, Baskerville, Pickering, and Whittingham, in England. A bibliomaniac will pay for an Elzevir cook-book several times its weight in gold. Caxton's, of which only about 650 are known, are almost unattainable. His "King Arthur" (1485) brought £1950 at auction on its quadricentennial.

6. The ban of church or state has enhanced many book values, though the Index Expurgatorius is good advertisement nowadays. Witness Fogazzaro in Italy last year. And the ban of all the good does not prevent the prurient from gathering their so-called "facetial."

A more extended résumé upon the subject of rare books may be found in Spofford's "Book for All Readers," New York (Putnams), 1900. With this caution, let us look at the dates of our collection.

The year 1770 is pretty nearly its center of gravity, about the same number of titles from the total of approximately 1000 being on either side of that date. Indeed one-half is crowded between the years 1750 and 1800. In the sixteenth century we have 33 titles; in the first half of the seventeenth, 37—a total of 70 reached by the year 1650. If now we count from this date by half centuries up to 1800, the totals fall into a rough geometrical progression with ratio of 2; while in the nineteenth century there are but 65 entries. As it is about the earlier volumes that I desire chiefly to speak, let me take you quickly over the few paces back of this date to the invention of printing, that we may appreciate their significance.

Without discussing block-books, produced in the fourteenth century and perhaps in the thirteenth, or entering for a moment upon the age-long controversy as to whether this honor belongs to Gutenberg of Mainz, Germany, or to Coster of Haarlem, Holland; or, as more recently claimed, to Waldfoghel of Avignon, France, and "stepping westward" with our faces away from China, be it sufficient for us to know that the earliest specimen of printing from movable types known to exist was the famous "Indulgence" of Pope Nicholas V in behalf of Cyprus, printed at Mainz in 1454, the first books issued here being two editions of the Vulgate not later than 1455, and the first dated book the Psalter of 1457. Then Italy started to print in 1465, Switzerland in 1468, France in 1470 (according to our best present information), the Netherlands in 1473 (as far as we may be sure), Spain in 1474, England in 1477 (her first printer being Caxton, whose motto, "fiat lux," Tennyson celebrates), Denmark in 1482, Portugal in 1489. Now by 1500 presses were operating in 50 towns of Germany, 71 of Italy, 6 of Switzerland, 41 of France, 22 of the Netherlands, about 25 of Spain, 4 of England, 5 of Denmark and the Northern countries, 23 of Portugal—an aggregate of 227 European towns in which printing was being done by the close of the fifteenth century. Hain (Repert. Bibl.) had listed up to the word "Ugniton," at his death, 16,082 works as published in the fifteenth century. The alphabet completed yields 16,299 titles. Some idea of the output may be gathered from the fact that in seven years' time the first press established in Italy printed 28 works in 11,475 copies. Now, if in this century, there were issued not 28, but over 16,000 works, we need not suppose, despite the gnawing tooth of time, that every volume antedating 1500 is a rarity; and Panzer (annales typographici—a far greater work than Hain's), who lists to 1536, certainly more than doubles this figure. It can be easily seen, therefore, that when our earliest volume, Joannes de Vigo, Opera in chyrurgia (1531), was issued, the number of single copies that had come from the press ran into the millions.

By this time books possessed the chief characteristics which mark them to-day. How many problems those first printers solved. Books were to be printed on rag paper. The sheets were to be folded and printed on both sides. A page was to be given to the title. Upon it or in the colophon were to be recorded the publisher's name, the place and date. Signatures and catch-words were there. The colophon was on the way to yield its functions to the title page. From the pomposity of Fust and Schoeffer in their first signed colophon (1457) is a long cry to the method of our earliest volume. Indeed I am not sure that we have another volume in which no portion of the imprint appears on the title page, all being given in the colophon. It is often the case that fuller information is to be found in the colophon, but the title page is not barren. So in one respect this volume does mark a transition period.

On the score of age, therefore, our collection's earliest volumes do not possess any extraordinary distinction. They are quite valuable, certainly, though I have not taken the trouble to run them down in trade lists to ascertain current quotations. Of course sixteenth century books in medicine do not grow upon trees. They are relatively but not absolutely rare. But as I have already indicated, books have more sources than content and age from which to acquire dignity and interest. One of these is the renown of the printer. We are fortunate in having a number of volumes which have come from famous presses, though not at the period of their greatest éclat. A few are worth mentioning with some detail.

The first is the Aldine press at Venice. There were three Aldines (more properly Manucci) of as many generations—Aldus Manutius, Paulus Manutius, and Aldus Manutius, Jr.,—printing from 1494 to 1597. We have two volumes from this press, Aetius Amidenus (1534) and Oribasius, one of twenty undated Aldines, but known to antedate 1555. These were both issued by Paulus Manutius, not the great founder, whose establishment is one of the most renowned in the history of printing. The death of the founder, occurring when his son, who was to succeed him, was a child, caused an interregnum of uncles, who let the property go down. Aetius was published in "in aedibus haeredum Aldi Manutii et Andreae Asulani," the year following the accession of the son, whose ambition it was to restore the fortunes of the house. This century of work was done in Venice. Venice was the home of more printers than any other city in Europe, and for this reason holds the highest place in the general history of printing. While not as interesting in the history of typography as some other cities, though even in this sphere, in conjunction with the Italian press in general, it has done us one unmeasured service, this city, fortified by the press of its country, is of supreme importance from a literary standpoint. The Renaissance movement, making itself felt throughout the fifteenth century, gained great impetus at the fall of Constantinople. Italy was then sole guardian of the ancient civilization; and fortunately its classics could

pour through her presses into the modern world. More than Queen Mary and Browning might say:

> "Open my heart and you will see
> Graved inside of it, 'Italy.'"

Venice is chief in this service, and her most celebrated son in the closing fifteenth and in the sixteenth centuries was Aldus Manutius. His plant was established mainly for the issue of Greek books. In 1500 he founded the Aldine Academy, the home of so many editors and the source of so many classics in the sixteenth century. Among others enrolled in this academy were Erasmus and Linacre. The device of this printer on his title page is an anchor, around which is curled a dolphin, and his motto, "festina lente." These were never wholly abandoned by the Aldines, until the expiration of their firm in the third generation. The invention of marks or vignettes is ascribed by Laire (Eudex librorum, saec. xv, ii, 146) to Aldus.

I said that Italy, and especially Venice, comparatively uninteresting for typographical history, had yet done one signal service in this field; and that was to fix in use the clear Roman type which we employ to-day in the mass of our printing. This came about in a curious but natural way. Typography was intended, as its name states, to "write with types," *i. e.*, to reproduce and multiply mechanically the current handwriting. Consequently its earliest models were the manuscripts which it printed. These hands would differ with localities, especially with countries. When, therefore, a printer set up shop in a town, he did not carry from the place of his apprenticeship a font of type already cast, but each cut one of his own to match the manuscript he was to reproduce, and these were mostly indigenous. This is almost universally true of the first quarter of a century of printing, and as the early printers so often had no place, date, or publisher indicated in title page or colophon, the study of types is the surest way of fixing in these respects the incunabula. (This method, by which each press is looked upon as a genus, and each product as a species—the natural history method—the method inaugurated by Panzer and well championed by the late Henry Bradshaw of the British Museum, stands in contrast with the method of Dibdin, who described books as curiosities, though Dibdin is still our greatest repository of facts.) So, the two earliest books from Mainz, Germany—the Mazarine and Bamberg Bibles, above referred to, appeared in Gothic type, which is still the national hand of Germany, though how great is the inroad of the Roman type one can see by a glance at current journals from that country. Now upon the introduction of printing into Italy, even though by two Germans, this custom prevailed; and as the scholarly scribes of this period had recently revived the Caroline minuscules of the eleventh and twelfth centuries, it was this beautiful hand which Italian printers reproduced in our Roman type. By the time that Caxton had been printing, say, three years in England (he began with Gothic), *i. e.*, by 1480, printers began to free themselves from the tyranny of the manuscripts, and in the resulting competition, Roman easily won.

The increasing demand also tended to lower prices from about this date, and as a result workmanship deteriorated. This became general by 1500. A shining exception to this rule again is Aldus. And I must not forget to mention that it was Aldus who introduced the use of Italics, said to be an imitation of the handwriting of Petrarch. This type was first used in his Vergil of 1500, though even here the capitals are Roman. We are all familiar with the subsequent narrowing field of this type. A complete register of the Aldine publications, arranged in chronological order may be found appended to the first volume of Ebert's Allgemeines Bibliographisches Lexikon, Leipzig, 2v., 1821-1830.

Schott.—From the press of the learned Strassburg printer of humanistic literature, and Luther's ardent supporter, Joh. Schott, we have an edition of Marianus & Albucasis (1532), our next oldest volume. He is especially noteworthy for his woodcuts, being the first to issue a modern atlas, and what the Germans call a "Situsbild," *i. e.*, a representation of the position of the human intestines, based on autopsy. This cut in Margarita philosophia, and one of the human skeleton, issued afterward as single sheets, spread everywhere and made a great impression, according to the Allg. Deutschr. Biog. (s. v.). In view of the historical value of these woodcuts, one should be well advised of the printer's various devices, which are often our means of recognizing his work.

Fraben.—One of the most important printers in Basel, the first Swiss town into which the art was introduced, and, for a while, surrounded by a group of reforming scholars, the most important in Europe, was Joh. Frobenius, the friend of Erasmus, whose support helped him to that textual accuracy, which, with his beautiful type, especially the Italic, enabled him to rival Aldus Manutius. At his death he was succeeded by his eldest son, Hieronymus, and his son-in-law, Nic. Episcopius, from whose house we have in our collection an Hippocrates (1538), and an Aetius Amidenus (1544).

Wechel.—Another protégé of Erasmus was Christian Wechel, who, with his son and successors at Paris, Frankfurt, Hanau, and Basel, printed from 1522 to 1629. The founder was one of the first to issue Greek and Latin texts in double columns and to get out parts of classical authors separately. While he does not rank as high as Estienne, he attained in Paris an eminent position in the book trade, both from the number and the technique of his issues. His son, Andreas, who succeeded him, sustained the high reputation of the name, but his outspoken Protestant views brought loss and peril, culminating in a bare escape with his life from the Massacre of St. Bartholomew's Night in 1572, when he fled with other Huguenot refugees to Frankfurt. It is from his greater establishment here that our Fernelius of 1577 comes, issued while the great Latin Bible of Tremellius and Jumis was in press. Our Dioscorides of 1589, and Falloppio of 1600 were issued by his sons-in-law, who succeeded him, Claude Marin and Jean Aubri. This firm is renowned for the editorial cooperation of Sylburg, from 1582 to 1591.

Giunta.—Another family of Italian printers was the

Giunta, originally from Florence. In the course of time descendants of it settled and printed in Italy, France, and Spain. Of the two brothers, Luca Antonio and Filippo, the former went to Venice and in 1530 established there a press of his own, which upon his death in 1537, passed into the hands of his son, Tommaso, who with his cousins published under the name of Haeredes L. A. de G. till 1657. From this press come our Galen (1609) and Mesue (1623). The work of this firm, however, which was most too much bent on profits, does not compare in excellence with that of the great Aldines. Ebert (op. cit.) in listing the publications of the Juntini's press in Venice concludes with the year 1592. Still it is worth noting that when in the third and last generation of the Aldines the prestige of their press had sunk, that of the Giuntas had at the same time been so gaining that this Aldus Manutius, Jr., sought to mend matters by marrying the great-grandchild of Giunta, the founder of the Venetian press. The fame of the Juntinis, however, rests upon the work of the other brother, Filippo, above referred to, and his sons, Benedetto and Bernardo, who operated in Florence. In both type and paper, the work of these two sons is but little inferior to the best Aldine production. The office closed in 1623.

Plantin.—Christophe Plantin (1514-1589) was one of the most famous of Dutch printers. In execution his work rivaled the best of his time, and many great engravers then flourishing in the Netherlands, illustrated his works. His son-in-law, John Moerentorf (Moretus), and descendants, continued to print in officina Plantiniana, though from the second half of the seventeenth century, the house began to decline. Our Forestus (1610) was issued many years after the founder's death by another son-in-law at Leyden, Francis van Ravelinghen (Raphelenguis), whom he had put in charge of a press, founded and operated by himself for a short time. In 1877 the city of Antwerp having bought the old buildings and contents, which had been kept religiously intact and enriched by the family, opened the Musée Plantin, the most remarkable typographical exhibit in existence.

Elzevir.—A fourth celebrated family was that of Elzevir, Dutch printers, whose activity extended from 1583 to 1712. The members are quite numerous, the most celebrated being Bonaventura, the son of the founder, who had his nephew, Abraham, for partner. The two members of this firm died within a month of each other in 1652, the date of our von Helmont and Jonston from the Elzevir press. They are, however, not the products of this most famous Elzevir firm, but, as also our Harvey, Exercitationes de generatione animalium (1651), were issued by Louis, the third of the name, and great-grandson of the founder. Our fourth Elzevir-Willis (1670), was the work of Daniel, son of the famous Bonaventura, and cousin of the Louis just mentioned, and the latter's partner from 1655 to 1662, after which date he printed alone. While reputed for their classics, the Elzevirs did not equal the Greek and Hebrew impressions of the Aldines in Venice. Their books are more celebrated for the elegance of their types and beauty of paper, than for their critical preparation. Their chief fame rests on their collection of French authors on history and politics in 24 months, known as "Petites Républiques." The family published in all 1213 works, of which 968 are in Latin, 44 in Greek, 126 in French, 11 in German, 10 in Italian, 32 in Flemish, and 22 in the Oriental languages. Their best issues are highly valued, but our three do not belong in this class.

Baskerville.—John Baskerville (1706-1775), footman, calligrapher, stone-cutter, decorative painter, japanner, tamer of a shrew, "terrible infidel," yet the printer of three Bibles, nine Common Prayers, two Psalm Books and two Greek Testaments; "illiterate," but at the commencement of his career announcing: "It is not my desire to print many books, but such only as are books of consequence, of intrinsic merit, or established reputation," and doing so for the sixteen or seventeen years of his publishing, mostly at his own risk, in the issue of Milton, Addison, Congreve, Shaftesbury, Ariosto, Vergil, Juvenal, Horace, Catullus, Tibullus and Propertius, Lucretius, Terence, Sallust, and Florus—John Baskerville, "the British Aldus Manutius and finest printer of modern times," is represented in a volume presented to this collection by The Royal College of Physicians of London—Wm. Hunter's Anatomia uteri humani gravidi (1774). This letter-press is the only medical work which Baskerville issued and one of the latest produced under his care, since he died the next year. It is an elephant folio illustrated with splendid line engravings by Strange and others. It was reprinted from lithographic transfers in 1828. In this volume we have a treasure, the *magnum opus* of a great man from a great press. Baskerville's high renown rests not so much upon the scholarly accuracy of his works as his wonderful type, ink, and paper. To secure a letter that would please his fastidious eye, he spent £600 and several years in experimenting. Dibdin (Introd. to the Classics, ii, 556), says: "He united, in a singularly happy manner, the elegance of Plantin with the clearness of the Elzevirs," though his type is calculated for an octavo or even quarto, being too slender and delicate for an imperial folio. The secret of making good ink had been a lost art in England for two centuries before Baskerville's experiments. He got a liquid of a "peculiarily soft lustre, bordering on purple," as Dibdin says again (l. c.). To his paper and ink, his enemies paid an unwitting compliment when they said that "whenever they come to be used by common pressmen and with common materials, they will lose of their beauty considerably." (Nichols, Illustrations I, 813). For a list of his publications, see Tedder, Dict'y of Nat. Biog. (s. v.).

While the name of the great anatomist is on our tongues, I cannot refrain from giving you a peep behind the curtain afforded by a homely-looking volume in this collection. The Scotch surgeon, John Douglas, issued a little "Treatise on the Hydrocele," upon which an anonymous critic under the title "Remarks on Dr. Douglas' Treatise," etc., and an "Answer" from Douglas appeared in quick succession. Upon

a fly-leaf in the back of these three pamphlets which we have bound together, some one, perhaps contemporaneous and at least stirred with choler at the lack of reverence to greatness, has penned the following note: "There was a reply to this answer with the author's name published soon after poor Douglas was dead: I think by one Justomand (Justamond), but it was a paltry performance like his remarks and not worth having. It is said Dr. Hunter put this young fellow upon making remarks upon Mr. Douglas because he happened to be a reader in anatomy." As a penalty, this youth is excluded from the Dictionary of National Biography.

Field.—I close this consideration of great printers whose work is represented here, by citing two titles which will show what interesting results might come from investigating the printers alone in these books. Cogan, Haven of Health (1596), and Barrough, Method of Physick (1601), were printed by Richard Field at London. The volumes themselves, aside from their early date, would hardly cause one to pause over them. And Richard Field—perhaps you have never heard of him before. If you look him up, you will find that he was an apprentice of Thomas Vantrollier, who printed North's translation of Plutarch's Lives in 1579; that upon his master's death in 1587 he acquired his interest in this and other interesting publications; that he held all the offices of honor in the Stationers' Company. And yet, though we read further that he built up a "highly valuable and dignified connection," we have not yet struck fire from the flint, and he is not one of the great ones. But one more fact will make us take a fresh grip on our old Haven of Health. Its printer, Richard Field, was the fellow townsman of William Shakespeare and the printer of the first (1593), second (1594), and third (1596), editions of his first (?) poem, "Venus and Adonis," as well as of the first edition of his "Lucrece" (1594). So that in the same year in which he issued our Cogan, Field was setting up copy for "the first heir of my invention," as Shakespeare styled it. Who knows but what the master dramatist, in visiting the printer's shop to talk over the third edition of "Venus and Adonis," picked up and fingered the leaves of this very copy of Cogan? The poet's and printer's fathers had been friends and neighbors in Stratford-upon-Avon. When the elder Field died, it was John Shakespeare, the poet's father, that attested in accordance with the custom a "a trew and perfecte inventory" of all his goods and chattels. When the "Venus and Adonis" was to be printed, what more natural than for the young poet to hunt up his old neighbor to do the work, especially as he had meanwhile been making good headway in London? Of this, as of the remaining first quarto edition of Shakespeare's poems and plays, our University library has facsimiles.

St. Paul's Churchyard.—We should perhaps get pickings rich enough if we had patience to pry into these old imprints. For example, in scores of these books, we meet here a phrase running something like this: "Printed (or sold) by ———, at the sign of the Lamb (for instance) in St. Paul's Church-Yard." Now this was a well-known booksdealer's quarter of those days. The history of this section is intimately connected with that of early English printing. For a great many years after its foundation, the output of the English press was extremely scanty, and almost entirely of popular character. It is Gibbon's sneer at Caxton that he never printed a classic. The best manuscripts and workmanship were to be had abroad, and the foreigner could undersell the native. This continued on into the sixteenth century. Indeed up till about 1516, with the exception of Caxton and Hunte, the Oxford bookseller, not one English name as printer or bookseller is found in the colophon of a book printed in or for England. But when the revival of letters became more felt and the demand for books consequently increased, the native trader began to feel more keenly foreign competition, and set about meeting it. In addition to legislative enactment curtailing the foreigner's privileges, his method was concentration of business. In St. Paul's Churchyard, where the denizen, perhaps because of liberties afforded him there from the stationers' companies, had early congregated, English shops were also then rapidly set up, till the yard became the beehive of the book trade. In the Sarum Missal of 1500, printed by Dupré, we meet for the first time with the statement that it was to be "sold by the booksellers in St. Paul's Churchyard." Here each shop had out a sign, some design which, with the name of St. Paul's, constituted the owner's address. Thus those of us who wish a copy of Margarita Chirurgica find ourselves reaching for the "Sign of the Spred Eagle, in Paul's Churchyard, near the great North doore," or in Latin we might be trying to reach "ad insigne Cygni Albi in Divi Pauli Caemitaerio." Hippocrates could be had either "at Mr. Bayle's Head" or "at Lord Bacon's Head." But you might get just as good at Homer's Head, Plato's Head, Cæsar's Head, Tully's Head, Horace's Head, Milton's Head, Pope's Head, Sir Isaac Newton's Head, or Turks' Head. But surely a more reliable dealer would be found under the sober signs of the Bible and Sun, Bible and Crown, Black Swan and Bible, Cross Keys and Bible, Angel and Bible, Angel and Crown or the Holy Ghost. Or, if the gift season be at hand, who could scout the artistic appeal of the Peacock, Lamb, Red Lion, Golden Pelican, Brazen Serpent, Swan, Buck, Three Pigeons, Bell, Golden Ball, Ring, or Star, swung out here and elsewhere? Sometimes this shop-sign, it appears, was also the printer's device entered on his title page. We have several neat examples in our list. The Rose may be seen in Freind, Prælectiones chymicae; the Lamb (*ibid.*), Emmenologia; the Swans in Menjot, Diss. pathol.; the Dôves in Ballonius, Consiliorum medicinalium, libri ii; the Bible and Crown, in Strother, Experienc'd measures. The signs could doubtless be changed at will. But a good one was perhaps a valuable asset; so that if a printer secured property bearing such a sign, he would keep it. They seem, however, to have belonged to the printers, who could take them when they changed quarters. There was apparently no copyright, since we find three persons living at the sign of the George at one time.

Those mentioned above I selected from the imprints in the Marburg collection. A complete list of London signs before 1558 may be found in E. G. Duff's "Century of the English Book Trade," London, 1905 (Bibl. Soc.), from which many of the facts just given have been drawn.

So much for the printer, his shop and his sign. But of course, books are here which have many other sources of interest than their issue from famous offices, or the authority of their authors in medicine—a field which Dr. Welch has already surveyed. I shall choose but four volumes, all except the first being from the seventeenth century, to each of which an interesting record adheres.

1. Linacre's Galen.—The first of these is Linacre's Latin translation of Galen's De Temperamentis (1521), as reproduced in facsimile in 1881 with an introduction by Dr. Joseph Frank Payne, librarian of the Royal College of Physicians, which added to the Marburg collection a number of titles, especially Hunter's Human Gravid Uterus, issued by Baskerville, above referred to. The original, which was the sixth book ever published by the Cambridge Press, can with difficulty be secured for $200. This volume has a distinction worth mentioning. It was the first book in England to employ cast Greek type, though there are very few Greek words retained from Galen. Greek type was introduced into England two years before, but it was inserted by woodcut. In Edinburgh, as late as 1579, the space for Greek words was left blank and afterward filled in by hand. Greek type had first occurred in Cicero's De Officiis, printed at Mainz in 1465 by Fust and Schoeffer; and a book entirely in Greek had been printed in Milan by Paravisinus as early as 1476, viz.: Lascaris, Greek Grammar.

2. Holland's Pliny.—Philemon Holland's translation of Pliny's Naturall Historie (1601) is an editio princeps of rarity and value, and the most popular of his voluminous renderings. Philemon Holland, who, by the way, died at the age of 85 without ever having worn spectacles, is termed the "translator general in his age," and all his versions are faithful and readable. Besides Pliny, he translated Livy (his first work), Plutarch's Morals, Suetonius, Lives of the Caesars, Ammianus Marcellinus, Camden's Brittannia and Xenophon's Cyropædia. A manuscript of Euclid's Harmonics—a beautiful piece of Greek calligraphy—written by Holland, was borrowed by Baskerville when preparing his Greek font. Our copy of his Pliny has lost the lower half of the title page, so that the imprint is here missing, but a colophon gives the needed information.

3. Burton's Anatomy.—Burton's Anatomy of Melancholy belongs to a class of books denominated ana, containing the sayings and doings of men great in their day. This book fell into neglect after the popularity greeting the first of such publications subsided, and then from being a mere waste-paper book, became extremely rare till reprinted in recent times. Ours is a beautiful copy, though the eighth edition of 1676, the editio princeps belonging to the year 1621.

4. Harvey Exercitations.—In our enthusiasm over Dr. Osler's gift of the editio princeps of Harvey's "De Motu Cordis," we have failed to notice another Harvey title of scarcely less interest than that opusculum aureum, as von Haller called it.

"At Christmas, 1650, Dr. George Ent visited Harvey at his brother's house, and after a conversation which is recorded by Ent, brought away the manuscript of a treatise entitled 'Exercitationes de Generatione Animalium, quibus accedunt quædam de Partu, de Membranis ac Tumoribus Uteri et de Conceptione." This was published in 1651 by Pulleyn in St. Paul's Churchyard, London. The parts of the hen's egg and the growth of the chick within it are fully described, and all the points of growth and development discussed in relation to it." (Moore, Dict'y of Nat. Biog., s. v. Harvey). This work, Harvey's last, except some letters, issued at the age of 73, six years before his death, was at once re-issued in the same year, 1651, by Elzevir at Amsterdam, and again in 1668 and 1674; at Padua in 1660; at Hanau in 1680, and at Leyden in 1737. Of the first Amsterdam edition we have a copy, as already noted. But more interesting is it that in 1653 it was published for the same Pulleyn, with a preface by Ent and a portrait of Harvey, in an English translation under the title "Anatomical exercitations concerning the generation of living creatures: to which are added particular discourses, of births, and of conceptions, etc." With respect to this book W. C. Hazlitt (Bibl. Coll. and Notes on Early English Literature, 2d ser., s. v. Harvey) remarks: "It is said that only 150 copies were printed, and of these 115 destroyed by fire." We have now one of these 35 in good condition, though the portrait has been abstracted, and in re-binding the margins have been shaved. In a recent catalogue of "First editions of one hundred famous books from Homer to Tennyson," J. Pearson & Co., of London, offered a copy in the original calf for 30 guineas.

There are doubtless numerous volumes of no mean bibliographical interest which I have passed over in ignorance or haste. But perhaps some more just perspective has been gained, as we shall approach these issues up to the middle of the seventeenth century, or shall in the future add to them. I felt that many of us, like myself, could be best served at this time by an extended caution regarding the early press. The list of works in the collection up to 1650 I here append for future reference. In this list Harvey (1628) is the gift of Dr. William Osler; and Aldrovandi (1642), Ballonius (1635-36), Farestus (1634), and Harvey (1648) are additions made by the Royal College of Physicians of London. The order is chronological.

Vigo, J. de. Opera . . . . in Chyrurgia. Additur Chyrurgia Mariani Sancti Barolitani. [Lugduni, 1531]. S.

Horatianus, O. Rerum medicarum libri quatuor [etc.].

Albucasis. Libri tres. Argent, 1532. F.

Aetius Amidenus. Librorum medicinalium tomus premius [etc.]. Venetiis, 1534. Q.

Puteanus, G. Ioannis Mesul aloen aperire ora venarum, aliaque similia non pauca dicenda, adversum I. Manardum [et al.], defensio [etc.]. Lugduni, 1537. S.

Galenus, C. Opera omnia [etc.]. Basileae, 1538. 5v. F.
Hippocrates. Libri omnes [etc.]. Basileae, 1538. F.
Budé, G. De curandis articularibus morbis commentarius. Parisiis, 1539. S.
Fuchs, R. Plantarum omnium quarum hodie apud pharmacopolas usus est magis frequens nomenclaturæ [etc.]. Parisiis, 1541. S.
——. Historia omnium aquarum que in communi hodie practicantium sunt usu [etc.]. Parisiis, 1542. S.
Aetius Amidenus. Medici Graeci . . . . id est sermones XVI per Ganum Cornarium . . . . latine conscripti. Basileae, 1542. F.
Vigo, J. de. Workes [etc.]. [London], 1543. Q.
Vidius, V. (Guido, G.). Chirurgia e graeco in latinum conversa [etc.]. Lucetiae Parisiorum, 1544. F.
Fuchs, L. Apologia [etc.]. Basileae, 1544. S.
Galenus, C. Ars medica . . . . M. Acakia interprete [etc.]. Lugd., 1548. T.
Oribasius. Collectorum medicinalium, libri XVII . . . . I. B. Rosario . . . . interprete. Venetiis [before 1555]. S.
Trallianus, A. Medici libri duodecim, graeci et latini . . . . I. Gumiterio Andernaco interprete [etc.]. Basileae [1556]. D.
Cassius Dio Cocceianus. Romanae historiae libri . . . . XXVI [etc.]. Lugduni, 1559. S.
Avicenna. Libri in re medica omnes [etc.]. Venetiis, 1564. F.
Rorarius, N. Contradictiones, dubia et paradoxa in libros Hippocratis, Celsi, Galeni, Aetii, Aeginetae, Avicennae cum eorundem conciliatonibus. Venetiis, 1566. S.
Paracelsus, P. A. T. Chirurgia . . . . a I. Dalhemis latinitate donata. Argent, 1573. 2v. in 1. F.
Fernelius Ambianus, J. Universa medicina [etc.]. Francofurti, a. m., 1577. F.
Plinius Caecilius Secundus, C. Historia mundi naturalis [etc.], a. m., 1582. F.
Gesner, C. Bibliotheca [etc.]. Tiguri, 1583. F.
Paulus Aegineta. Opera, I. Guniterio Andernaco . . . . intreprete [etc.]. Lugd., 1589. S.
Clowes, W. A proved practice for all young chirurgians [etc.]. [London], 1591. D.
Cogan, T. The haven of health [etc.]. London, 1596. D.
Pinaeus, S. Opusculum physiologum et anatomicum [etc.]. Parisiis, 1597. S.
Guillemean, J. The Frenche chirurgerye . . . . tr. . . . . by A. M. Dost, 1597. F.
Dioscorides Anazarbeus, P. Opera quae extant omnia ex nova interpretatione Jani-Antonii Saraceni [etc.]. N. P., 1598. D.
Phenice (Fenice)—Canal, Dictionaire françois et italien [etc.], [and] Dittionario italieno et francese [etc.]. N. P., 1598. D.
Falloppio, G. Opera omnia [etc.]. Francofurti, 1600. F.
Plinius Caecilius Secundus, C. The historie of the world . . . . tr. . . . . by P. Holland. London, 1601. F.
Barrough, P. The method of physick [etc.], 3. ed. London, 1601. D.
Commentariorum Colligii Conimbricensis Societatis Iesu in octo libros physicorum Aristotelis [etc.]. Coloniae, 1602, 2 pts. in 1 vol. O.
Rudius, E. De ulceribus libri tres. Patavii, 1602. D.
Minderer, R. De pestilentia [etc.]. [Vindobonae, 1608, ?]. S.
Quercetenus, J. Pestis alexicacus [etc.]. Lipsiae, 1609. S.
Galenus, C. Opera ex octava Guntarum editionie. Venetiis, 1609. 5 v. and index. F.
Forestus Alemarianus, P. Observationum et curationum chirurgicarum libri quatuor posteriores [etc.]. [Lugd. Batev.], 1610. S.
Margarita chyrurgica . . . . by S. H. London, 1610. S.
Salerno. Scuola. Medicina Salernitana [etc.]. Francofurti, 1612. T.
Mesue Damascenus, J. Opera [etc.]. Venetiis, 1623. 2 v. in 1. F.
Mercurialis, H. Medicina practica [etc.]. Lugd., 1623. Q.
Jacchaeus, G. Institutiones medicae. Lugd., Batav., 1624. T.
London. Royal College of Physicians, Pharmacopœia Londinensis . . . . tertia ed. [etc.]. London, 1627. Q.
Harvey, W. Exercitatio anatomica de motu cordis et sanguinis in animalibus. Frankfurt, 1628. Q.
Charron, P. Of wisdome three bookes.—Tr. by S. Lannard. London, [1630]. D.
Burgersdicius, F. Idea philosophiae moralis [etc.]. Oxoniae, 1631. T.
——. Idea philosophiae naturalis [T. p., lost. Bd. w. preceding.]
Guybert, P. Le medicin charitable [etc.]. Paris, 1632. T.
Gerard, J. The herball, or generall historie of plantes . . . . Enlarged and amended by T. Johnson [etc.]. London, 1633. [or 1636. T. p. lost]. F.
Hippocrates. Aphorismi, soluti et metrici, interprete J. Heurnio, metaphrastis J. Frero et R. Wintertons. Cantabrigiae, 1633. T.
Forestus Alemarianus, P. Observationum et curationum medicinalium ac chirurgicarum opera omnia [etc.]. Francofurti, 1634. F.
Lowe, P. A discourse of the whole art of chirurgerie [etc.], 3 ed. London, 1634. D.
Poetae Minores Graeci [etc.]. Cantabrigiae, 1635. S.
Hartmann, J. Praxis chymiatrica [etc.]. Genevae, 1635. S.
Ballonius, G. Consiliorum medicinalium, libri ii [etc.]. Parisiis, 1635-36, 2v. in 1. Q.
Woodall, J. The surgeon's mate [etc.]. London, 1639. F.
Plater, F. Observationum in hominis affectibus plerisque corpori et animo, functionum laesione, dolore, aliave molestia et vitio infensis, libri tres [etc.]. Basileae, 1641. S.
Sennert, D. Opera. Parisiis, 1641, 3v. F.
Aldrovandi, U. Monstrorum historia [etc.]. Bononiae, 1624. F.
Galenus, C. Epitome Galeni operum . . . . auctore A. Lacuna. Lugd., 1643. F.
Primrose, J. De vulgi erroribus in medicina, libri iv. Amstelodami, 1644. T.
Schenck à Grafenberg, J. Observationum medicarum rariorum, libri vii [etc.]. Lugduni, 1644. F.
Ranchinus, F. Tractatus duo posthumi [etc.]. Lugduni, 1645. D.
Fabricius Hildanus, G. Opera quae extant omnia [etc.]. Francofurti, A. M., 1646. F.
Harvey, W. Exercitatio anatomica de motu cordis et sanguinis . . . . Accessit diss. de corde J. de Back. Roterodami, 1648. T.
Sebizuis, M. De alimentorum facultatibus libri quinque [etc.]. Argent., 1650. D.

But with the bars down, one may spend a pleasant hour browsing over such elaborate title pages or frontispieces, not to mention photogravures and illustrative woodcuts, as are to be found in works by such authors as Albertus Magnus, Barbeth, Barry, Blancard, Borellus, Brugis, Charron, Cheselden, Dionis, Douglas, Eustachius, Fabricius **ab Aquapendente**, Fibricius Hildanus, Galenus, Greenhill, Guillemean, van Haller, Harvey, Horstius, King, La Condamine, Le Clerc, van der Linden, Lowe, Menjot, Muys, Nuck, Poole, Quincy, Russell, Ruysch, Sebizius, Severinus, Sibley, Tulp, Willis, Zwelfer, etc.

And even to the student who merely reads the list of author's names a pittance of pleasure and profit will not be denied. In the Middle Ages (and to a certain extent in

the Renaissance and Reformation periods), the Latin language was the universal medium of communication. The writer would Latinize his name also. For the most part, this meant merely to give it a declausional form, the Mundinus de Lentiis is a little removed from Mondino da Luzzi, Christophorus de Questis from Honestus, Vidus Vidius from Guidi Guido, and Bruno from Brown; as elsewhere Copernicus from Zepernik, and Camerarius from Kämmerer. But if the name had a common signification, it was translated into Latin or into Greek with a Latin termination. Thus, Du Bois appears as Sylvius, Hagenbut as Cornarius, Holtzmann as Xylander, and elsewhere Schlüssel as Clavius, Kopflein as Capito, Hausschein as Oecolampadius and Rauchfuss as Dasypodius. Similarly men soon wearied of telling an Arab's pedigree in his name, "long drawn out" enough but hardly "lengthened sweetness," and so a Latin form was substituted. Avicenna is perhaps here to stay for Ibu Sina; and one would hardly have the temerity to suggest that we displace Rhazes with Muhammad Ben-Zacharia Abu-Bekr Al-Razi, or Mesue with Jahja Ben Maseweih Ben Ahmed Ben Ali Ben Abd el-Malik.

Curios are doubtless frequent in the collection. Christopher Nugent has a naive way of stating his proposition which may be recommended to Dr. Cushing's corps of family physicians: "An essay on the hydrophobia: to which is prefixed the case of a person who was bit by a mad dog; had the hydrophobia; and was happily cured." It is a modest soul who withholds his name from the following offering: "The way to health, long life and happiness, or, a discourse of temperance and the particular nature of all things requisite for the life of man, as all sorts of meats, drinks, air, exercise, etc., with special directions how to use each of them to the best advantage of the body and mind. Showing from the true ground of nature whence most diseases proceed, and how to prevent them. To which is added, a treatise of most sorts of English herbs, with several other remarkable and most useful observations, very necessary to all families. The whole treatise displaying the most hidden secrets of philosophy, and made easy and familiar to the meanest capacities, by various examples and demonstrances. The like never before published. Communicated to the world for a general good, by Philotheos Physiologus." But two will not be shaken from my memory soon—the one because our copy has lost its title page and hence I had to read its startling theories in order to trace its author; the other because the title page is present, and very much so. I refer in the first instance to Sir John Hill's burlesque of the Royal Society—"Lucina sine concubitu," etc., published under the nom de plume Abraham Johnson; and in the second to the work of John Snart, who does so in the following title page: "Thesaurus of horror; or, the charnel-house explored!! Being an historical and philanthropical inquisition made for the quondam-blood of its inhabitants! by a contemplative descent into the untimely grave! Shewing, by a number of awful facts that have transpired as well as from philosophical inquiry, the re-animating power of fresh earth in cases of syncope, etc., and the extreme criminality of hasty funerals: with the surest methods of escaping the ineffable horrors of premature interment!! The frightful mysteries of the Dark Ages laid open, which not only deluged the Roman Empire, but triumphed over all Christendom for a thousand years! Entombing the sciences, and subsequently reviving all the ignorance and superstition of Gothic barbarity."

"κόνφη σκιά, καὶ ἀτμὶς ἐστιν ἀνδρῶν βιος"

"I could a tale unfold, whose lightest word would harrow up thy soul," etc.—*Shakespeare's Hamlet.*

"But if the fertilizing earth restore
The dubious fragment of a borrow'd life,
Can man's most desp'rate scuffle force the grave,
Or must he, grappling, bathe himself in blood,
And burst his eye-balls in the vain attempt!!!"

NOTE.

NEW YORK STATE COMMISSION TO INVESTIGATE THE CONDITION OF THE BLIND.

Batavia, N. Y., December 15, 1906.

My Dear Sir: The loss of sight in the case of an individual is of economic importance to the State. The New York State Commission to Investigate the Condition of the Blind has been charged, therefore, by the Legislature with the duty of inquiring into the causes of blindness, and of recommending methods by which, as far as possible, unnecessary blindness may be prevented. To that end the commission begs the assistance and advice of the medical profession. The secretary will gratefully receive and acknowledge any reprints, reports, pamphlets—or personal communications bearing on the causes and prevention of blindness.

More especially information is sought on the following points:

Congenital blindness.—Its causes, the influence of heredity, consanguinity, etc. The reports of cases of blind parents producing blind children, character of blindness in such cases, etc.

Ophthalmia neonatorum.—How generally are preventive measures employed? Statistics bearing on the subject. What silver salt and in what strength should be recommended?

Trachoma and other infectious eye diseases.—Statistics. How may early treatment be secured? Prevalence in schools, orphan asylums, etc. Preventive measures—medical inspection of schools.

Blindness from accident, injuries, fireworks, toy-pistols, etc.—Statistics. Method of protection for eyes of workmen and others. Prohibition of dangerous explosives at celebrations.

Toxic amblyopia.—From methyl alcohol—other toxic agents. How may the public be protected?

Neglect on the part of patients visiting dispensaries.—Patients suffering from conditions threatening vision absent themselves from clinics after being advised of the need of immediate treatment until too late. Method of reaching such.

Blindness due to neglect of slight ophthalmic injuries.—How can early treatment be more generally secured?

Blindness due to improper hygiene and sanitation in corneal troubles of children.—How can early treatment be secured?

Other causes of blindness.—Suggestions as to prevention.

The commission will be most grateful for advice and assistance on the above subjects. Very respectfully yours,

F. Park Lewis, President, 454 Franklin St., Buffalo.
O. H. Burritt, Secretary, Batavia.

ON A METHOD OF PRESERVING OUTLINES OF VISCERAL LESIONS ON NAINSOOK OR SUISSE MATERIAL.

By Howard A. Kelly, M. D.

In the year 1883, I published an article in the *Medical News of Philadelphia* (vol. 43, p. 417), "On the Mapping Out of Visceral Diseases, in an Aniline Color, on the Surface of the Body," describing a practice which I had *introduced* into my wards during my residency in the Episcopal Hospital of Philadelphia. My desire was to secure a graphic representation of pulmonary, pleural, and abdominal conditions in color on the skin of the body, to serve as an ocular demonstration in teaching, as well as to promote the more accurate study of my cases by furnishing an accurate basis of comparison in measuring the changes which might occur from day to day, or week to week. I well remember the amused interest of my chief of the ward, when he lifted the night-dress of a case of pleural effusion and saw the limits of the effusion mapped out in purple on the chest wall. It was soon after this time that this method came into general vogue, both in this country and in Europe, as a valuable adjuvant in the clinical amphitheatre. The idea was too simple and the advantages too obvious to escape the attention of the profession long after the invention of the aniline pencils, and I am not even yet aware whether my own communication was the first upon this subject or not; I can only assert that it was original with me in the year 1883 when I was a hospital resident.

Of late years I have been much impressed with the importance of making more accurate records of the examinations in our gynecological surgical cases; and I have felt in particular that it was desirable to work out some plan of making accurate pictorial records which could be filed away for comparison from time to time. In demonstrating a case, nothing is so impressive as a record which contains both a written description, and, at the same time, an appeal to the eye by means of an accurate pictorial representation. In the early nineties, with these ends in view, through the kind help and skill of my friend, Mr. A. S. Murray, between fifteen hundred and two thousand photographs of patients, of operations, and of specimens were taken in the gynecological service of the Johns Hopkins Hospital. It was at this time that Mr. Murray invented the vertical photographic apparatus to take specimens which could not so well be hung up. These records proved invaluable in the years that followed, as they formed the basis of many of the drawings and illustrations used in our various publications.

The method of describing an abdominal tumor commonly in vogue is, to outline it by palpation, and then to measure its various diameters projected on the ventral surface of the body, in addition to measuring the distance from the periphery of the tumor out to the various fixed points in the abdomen, such as the symphysis pubis, the anterior superior spines, the umbilicus, and the margins of the ribs. In the case of uterine fibroids, I have also long used a pelvimeter to determine the extreme length of the tumor, by placing one arm of the pelvimeter in the vagina on the cervix, and the other on the outside against the abdominal wall on top of the tumor.

These methods are of great value, but they still leave much to be desired, and I think I have attained one further desideratum, in the form of a pictorial record, which is made upon a transparent stiff tissue, laid over the abdomen, upon which the surface markings seen beneath are easily transcribed. More minutely the procedure is as follows: The case is carefully examined, and the tumor or displaced organ, whether a kidney, stomach, uterine or ovarian growth, is carefully outlined on the surface of the abdomen by means of an aniline pencil. I do this commonly by palpating, and following the palpating finger by a series of aniline points on the skin, made about an inch or half an inch apart, thus outlining the tumor or organ on all sides, as the patient lies on her back, with the limbs slightly flexed. Then with the assistance of the nurse, or perhaps of the patient's hands, the transparent tissue on which the record is to be made is laid upon the abdomen and held steadily in one position. The examiner then marks on the tissue the anterior superior spines, the symphysis pubis, and the umbilicus, by means of rapid strokes with an aniline or crayon pencil. Next the tumor is carefully sketched, connecting the points on the skin, seen through the tissue, by a continuous line. After this, the margins of the ribs are outlined, and the breasts, if desired; the outline of the body and the upper thighs, with the crease of the thighs may be added. To get the outline of the body, I hold the tissue out straight from the body, and then looking vertically downwards, sketch on it the outline as seen through the material. If the patient comes back at a future date for a comparative examination, as for example in the case of a fibroid tumor, which may be increasing in size, a similar examination and similar measurements are made independently of the first. The new record is then superimposed upon

Fig. 1.

Fig. 2.

Fig. 1.—Palpating an ovarian cyst seen in sagittal section. The fingers of the left hand rest on the lower pole of the cyst, while the right hand is engaged in determining the limits of the tumor as felt through the abdominal wall. By a succession of short, rapid strokes with the fingers, a sort of vibrating thrill is communicated to the tumor and felt by the vaginal fingers. This is a much more delicate way of outlining a mass than by the usual method of palpation. The rapid succession movement is illustrated in the diagram by making several fingers appear in the place of one.

Fig. 2.—The tumor is first mapped out with an aniline pencil or the skin sprayed with alcohol, at points an inch or more apart, a^1, a^2, a^3, etc. Then a series of further markings are placed between each of these at b^1, b^2, b^3, etc. After this the lines may be connected.

the one first made, when it is easy to determine at once whether there has been any increase or not.

The cost of the nainsook material is, at retail, sixty cents a yard; it is one yard wide, and each yard makes eight pieces large enough to cover the abdomen. The Suisse material costs thirty cents a yard, but is just about one-half as wide again as the nainsook, so the cost is about the same. A close meshed cheesecloth stiffened with starch could be used; this would be much cheaper. The nainsook tissue can be boiled and sterilized and used over the open abdomen, if desired, but in this case it loses its stiffness.

For class demonstration, the records can be fastened on large pieces of white cardboard, which serve to throw the black outlines into prominence.

I observe that sketches made in this way have an individuality never seen in the sketches made in the memoranda of a casebook. This is seen particularly in the outlines of the costal margins, all of which differ. I think it is a great advantage, too, to be compelled, in this way, to spend a longer time in examining the patient. It is also a means of inspiring confidence in the patient, who realizes that the examiner is giving minute attention to the particular circumstances of her case.

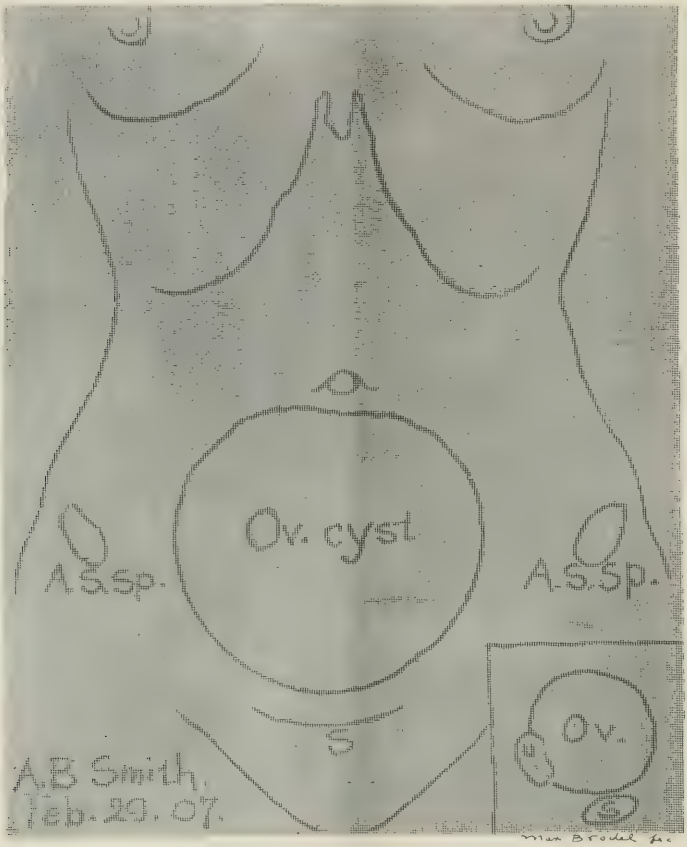

FIG. 3.—The gauze record of the abdomen and its contents. These markings are traced on the gauze material laid on the abdomen with a crayon or black pencil. The name of the patient and any important data are written in one corner and in another corner is an outline in sagittal section of the relation of the uterus to the tumor. If the outlines are all traced on the skin first, a piece of glass can then be laid on the abdomen and with the gauze stretched on this a true geometrical projection can be made.

A CLINICAL STUDY OF MUSHROOM INTOXICATION.

By William W. Ford, M. D., D. P. H.,

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The celebrated French mycologist, Paulet,[1] himself a physician, has given us, in a delightful volume, "Traité des Champignons de France," published in 1793, a comprehensive study of the uses to which edible fungi may be put, and has emphasized the dangerous and fatal consequences of the consumption of the poisonous varieties. He points out that from time immemorial mushrooms have been sold, especially during Mid-Lent, in the public markets at Pekin, at St. Petersburg, at Florence, and in various smaller cities and towns in Hungary and Tuscany. Paulet comments with some sarcasm upon the knowledge of fungi shown by the peasants in these countries, and their ability to distinguish between the harmless and poisonous species, compared with the ignorance of the French of that epoch. Historically it is also a well-known fact that the ancient Babylonians and the early Romans employed mushrooms in great quantity, not only as delicacies for the tables of the rich, but as a daily food for the poorer classes. Indeed one of the most beautiful of all our wild species, a plant growing to a height of eight or nine inches, with a top or pileus expanding to a width of seven or eight, of a gorgeous reddish-brown or yellowish-brown color, the *Amanita cæsaria,* owes its name to the favor with which it was regarded by the early Roman emperors. Curious beliefs in regard to this name and species have survived in French literature, however, where occasionally one finds the statement that the name "Cæsaria" should properly be applied to the deadly *Amanita muscaria,* because of its use by the corrupt Latin rulers as a convenient and easy method of disposing of dangerous enemies.

At the period in the world's history when the value of food was necessarily estimated empirically, poisonous fungi were unavoidably consumed in great quantity from time to time, and ancient records attest that fatalities from these plants were by no means uncommon. One of the most interesting if not the earliest recorded case of mushroom intoxication is that experienced by the family of the Greek poet, Euripides. During his absence from home, on one occasion, it is related, in a single day, his wife, his two sons, and a daughter all died from the consumption of poisonous mushrooms.*

On the authority of Pliny, Paulet states, deaths from this cause were by no means uncommon among the consular families of Rome, and he cites among other notables who lost their lives in this way, Pope Clement VII, the Emperor Jovien, the Emperor Charles VI, Berronill of Naples, and the widow of the Czar Alexis. A curious story has come down to us concerning the death of the Emperor Claudius. It seems that this great man, desiring to rid himself of an uncongenial spouse, disposed of her by some one of the many ways open to him as a man of influence, and promptly took unto himself a younger, but alas, no better helpmate. The new selection failed to appreciate the kindly qualities of the Emperor, and according to some traditions, brought about his death by substituting deadly "toadstools" for his favorite edible mushrooms. To make things doubly sure, according to other traditions, mineral poisons were added to the fungi.

It is also related by Paulet that the young daughter of the Greek historian, Pausanius, was severely poisoned but eventually recovered and in Paulet's own century Madame, the Princess of Conti, nearly lost her life by mistaking *Amanita muscaria* for the edible *Amanita cæsaria.* Paulet himself was much impressed by the number of deaths in France, and states that from the year 1749 to 1788 there were a hundred deaths in the environs of Paris alone. Next to Paulet, the French mycologist, Bulliard,[2] did more than any other to systematize the knowledge of fungi possessed by men of that generation, and many of the names and species established by Bulliard are accepted by modern mycologists. To the small white or spring form of the "deadly Amanita," Bulliard gave the name "destroying angel," because of its extreme toxicity, and modern knowledge of this fungus has only served to confirm his observations. Since the time of Paulet and Bulliard, French scientists have many of them devoted much time and attention to the study of mycology and many papers, both popular and scientific in character, have been written on this subject. The various species of fungi have been accurately described, their alimentary value discussed, and the dangerous properties of the poisonous forms emphasized. Indeed in no other country to-day are mushrooms known and loved as they are in France, unless it be possibly in the sunny land of Italy. Many of the theses published by French mycologists are of permanent scientific value, and among them should be mentioned those of Cordier,[5] Bardy,[4] Gillot,[5] and Guillaud.[6] The "Société mycologique de France" was established in 1886 and its Monthly Bulletin is a mine of information to mycologists. In Germany the subject has been approached possibly more from the chemical and pathological standpoint, and a large number of fatalities have been analyzed. Numerous cases of poisoning have also been published in England and in this country. For instance, Palmer,[7] of Boston, collected 33 cases with 21 deaths, and Forster,[8] of Charlestown, 44 cases with 14 fatalities. Other statistics are those of Falck,[9] in Germany, including 53 cases with 40 deaths, of Bardy (l. c.), who reported 60 cases in that district of France known as "Les Vosges," and of Guillaud (l. c.), who estimated the

*Quoted by Paulet from Eparchides.

number of deaths occurring annually in the southwest of France at about 100. From these statistics it may be seen that the mortality from this source depends to a large extent upon the size and the needs of the peasant population. In Italy and France, for instance, and in certain parts of Germany, fungi are utilized in great quantity by the poor who either collect them for their own consumption or who bring them to the public markets where they command a high price for their value as delicacies. In these countries deaths from mistakes are not infrequent. Similar conditions prevail in Japan, where a large and indigent peasant population compels the use for food of nearly every plant that grows, especially during some of their devastating famines. Inoko,[10] for instance, has reported over 480 cases of mushroom intoxication during a period of eight years. Contrasted with these figures we find that in England and America, where there is no abjectly poor element in the population, the deaths from this cause are relatively few in number and belong to two distinct categories. On the one hand there are the frequent cases in which crass ignorance is responsible for the fatality, deadly fungi being picked and eaten because of their beautiful color, the victims possessing absolutely no knowledge of the properties of fungi or of the poisonous and edible species. On the other hand, many of the victims are foreign-born, natives of Russia, Poland, or Bohemia, who are perfectly familiar with the appearance of edible fungi at home but are deceived by the variations in color which the species present in other localities. A case in point is that of the Count de Vecchi, in Washington, who was supposed to be an expert on the subject of fungi, but who died from eating species containing muscarine, probably *Amanita muscaria.* In German, Italy, and France strict laws have now been passed regulating the sale of mushrooms, but fatalities occur regularly from what appear to be unavoidable errors.

In Canada and in the United States the loss of life annually from poisonous fungi is not great, unless we estimate the proportion of deaths from this cause to all the deaths due to accidental causes. During the summer of 1905 there were about 30 cases of poisoning with 12 deaths, and during the season of 1906 there were 15 or 16 deaths.

While mushrooms do not rank high in the scale of foods from their nutritive value, Möner[11] and Mendel,[12] having both pointed out that the amount of available proteid in them is surprisingly small, they possess a delicacy of flavor highly prized by epicures, and the cost of procuring them, at least in the natural state, is limited to the labor of collection. Furthermore, mushrooms contain in addition to albuminous material, such substances as sugars, starches, and easily decomposed glucosides, all of which may play a not unimportant part in maintaining the nutrition of the body. There is no reliable method of testing the edibility of mushrooms, an expert knowledge of species being necessary for all who would indulge in them. Drying does not destroy the toxicity of the poisonous varieties, the active principles in all cases being heat-resistant. It seems inevitable, therefore, that deaths should occur from time to time and it thus becomes a matter of much interest and some importance to discuss briefly the forms of mushroom intoxication and to put on record the fatalities from the various species. Gillot (l. c.), in 1900, collected over 200 authentic cases of poisoning, most of these occurring in France, and I have been able to find nearly as many more in the German and English literature, and in the French since 1900.

Poisoning by Amanita phalloides.

Amanita phalloides, known commonly as the "white" or "deadly Amanita," and the closely related species, "Amanita verna" (the destroying angel of Bulliard), is the cause of by far the majority of fatalities from mushroom eating. It has been described under a number of different names, such as *Amanita bulbosa,* Pers., and its varieties—*alba, citrina, virescens* and *olivacea, Agaricus bulbosus,* Bulliard; *Amanita viridis,* Pers.; *Amanita mappa, Amanita viresa,* Fries, and *Amanita venenesa,* Pers., while the terms *Amanita recucita,* Fries, and *Amanita porphyria,* Fries, probably indicate the same species. In French literature it is known as "l'oronge ciguë," "l'oronge blanche ou citronée," "l'oronge ciguë jaunâtre," and "l'oronge souris." In German it is popularly called "Knolblätterschwamm." The species indicated by these various names has a characteristic appearance and is readily recognized by ordinary collectors of fungi. It usually grows to a height of five to seven inches and it consists of a base or expended cup (the poison cup) upon, or more properly speaking, within which rests the stalk. The latter is surmounted by an expanded top or pileus on whose under-surface are attached the gills covered with white spores. The plant is pure white in color with the exception of the pileus, the upper surface of which varies from a china-white to an amber or pale yellow. Occasionally the top is greenish in color, especially in Europe, but the greenish plants are practically never seen in this country. The cup, the stalk, the under-surface of the pileus and the gills are always pure white with the possible exception of a few flakes of yellow rarely seen on the stem. The pileus is usually smooth but at times delicate flakes or scales easily removed by brushing lightly with the fingers, are found on the upper surface. The *Amanita verna,* regarded by many mycologists as merely the spring form of *Amanita phalloides,* differs from the latter only in size and color. This form is always pure white, has few or no scales on the pileus and grows to a height of but four to five inches. Much smaller forms are very abundant in the early spring, possibly the most common variety being a plant only about two and a half to three inches tall, with a pileus measuring only one to one and a half inches in diameter. In all these species the color of the spores may easily be ascertained by allowing the pileus to rest gills downward upon a sheet of paper or a piece of smooth wood. After the lapse of three or four hours the spores are deposited upon the wood or paper in a design representing the arrangement of the gills and with a color characteristic for each species.

This is the "spore print." Neither *Amanita verna* nor *Amanita phalloides* are difficult to recognize and both forms are very abundant all over the United States. I have collected them in large quantities, for instance, in the Blue Ridge Mountains of North Carolina, Maryland, and Pennsylvania, in the neighborhood of Woods Hole, Mass., and on the adjacent islands. They are furthermore very common in New York, Pennsylvania, and Ohio, and they apparently enjoy a universal distribution. Nearly all the cases of poisoning reported in this country during the past few years are due to these two species. Closely related species, such as *Amanita cothurnata* and *Amanita relatipes*, although differing from *Amanita phalloides* in certain morphological features cause an intoxication apparently identical with that due to the "phalloides" and evidently harbor the same poisonous principles.

The clinical symptoms of this form of intoxication are characteristic. A prodromal stage of six to fifteen hours in which no symptoms are observed by the victims is followed by a sudden attack of extreme abdominal pain accompanied by vomiting and diarrhœa. Vomitus and stools consist of undigested food with much blood and mucus. Anurea is usually present and rarely constipation is seen. Hæmoglobinurea has never been described, and in many cases specific statements are made as to the lack of coloring matter in the urine. Paroxysms of pain and vomiting alternate with periods of remission, the extreme suffering producing a Hippocratic facies characterized by the French as "la face vultueuse." The loss of strength is rapid and excessive. Jaundice, cyanosis, coldness of the skin, especially of the extremities, develop within two or three days, followed by profound coma and death. The course of the disease lasts four to six days in children and eight to ten in adults. Ocular symptoms and convulsions are rarely noted, but both may occur, the convulsions appearing as a terminal event more common in children than in adults. If large quantities of the fungus have been eaten a very profound intoxication develops and death may occur within 48 hours. The mortality in this form of intoxication is very high, varying from 60 to 100 per cent in different epidemics and death may follow the consumption of surprisingly small quantities. Plowright,[13] for instance, has reported the death of a child of ten years from eating one-third of the top of a small plant, and there are numerous deaths reported from eating one or two good-sized specimens. Cooking these fungi does not destroy their toxicity, the majority of accidents occurring with well cooked material. The strength of the poisonous principles is apparently lessened, however, since smaller quantities of the raw plant can produce a fatal result than when the plants have been thoroughly heated.

The cases recently reported by Pfromm[14] are so typical of nearly all the epidemics that they may well be quoted as representing the usual course of events. A family of Italians living near Philadelphia collected one Sunday a large quantity of mushrooms which they cooked and ate about six o'clock in the evening. The parents ate largely of the fungus, the two children merely dipping bread in the juice and eating the well-soaked bits. About midnight all members of the family were awakened by the most violent abdominal pain accompanied by vomiting, headache, and extreme thirst. The family was visited the following morning by a physician. He found the family all seriously ill, the father profoundly prostrated, cyanotic, with muscular twitching about the chest. The patient soon became delirious, with glazed eyes and contracted pupils. His symptoms were somewhat ameliorated during the day but towards evening they returned with equal severity. For a period of eight days periodical attacks occurred, finally resulting in coma and death. During the latter part of the illness the characteristic Hippocratic facies was present to an extreme degree. The mother suffered from corresponding symptoms, especially from the vomiting and thirst. She finally developed delirium and coma and died on the eighth day. During her attack she aborted a five-months fœtus. Several similar cases are on record. The two children went into coma after a period of excessive pain and vomiting, dying within an hour of each other, 57 and 58 hours after consuming the juice of the fungi. Specimens of the plants eaten were identified by botanists as *Amanita phalloides*.

Other cases of *Amanita phalloides* intoxication have been reported in this country, especially by Palmer (l. c.), Forster (l. c.), Trask,[15] and McIlvaine.[16] In France poisoning is not uncommon among soldiers on the march and in charitable institutions. The "Bulletin de la Société mycologique de France" has reported 18 fatalities since 1900. Probably the most horrible of all the epidemics reported in that country occurred in October, 1884, at the Orphanage of St. Louis, near Pont de la Maye, Gironde (Faure[17]). Here large quantities of *Amanita phalloides* were gathered by ignorant attendants, and being considered edible, were fed to the inmates of the institution on October 6. Between this date and October 10, a period of five days, eleven children died.

Schröter,[18] in 1885, also reported an epidemic with a high mortality, in Silesia, 10 of the 11 affected persons succumbing. Recovery after ingestion of small quantities of fungi may occur. In this event the individuals suffer extremely for a period of eight days to three weeks, but the severe symptoms gradually ameliorate, the patients gain strength and are eventually restored to normal health. The severity of the intoxication depends almost entirely upon the amount of material consumed and neither children, adults, or old people are exempt from fatal consequences.

The *active principle* of *Amanita phalloides* has been sought from early times, but our first knowledge of any value came from the investigations of Kobert.[19] In 1891 he described a hæmolytic poison in this fungus, considering it a "tox-albumin," and naming it "phallin." This substance he believed to be the active principle. Kobert modified his views in 1900,[20] when he described an additional poison of great strength which he stated to be an alkaloid. Subsequently

Ford [21] confirmed Kobert's early observations as to the hæmolytic substances in *Amanita phalloides,* but on the basis of biological experiments was led to believe that an active toxine existed in the fungus, and to this body he gave the name *Amanita-toxin.* It is probably identical with the so-called alkaloid described by Kobert. Recently Abel and Ford [22] have pointed out that the hæmolytic substance in this fungus is not proteid (toxalbumin) but an easily decomposed *glucoside.* This glucoside, because of its extreme sensitiveness to heat, to small traces of acid and to digestion by pepsin and pancreatin, can play no role in the intoxication in man where the cooked fungi are introduced into the stomach. The *Amanita-toxin,* which is resistant to heat, to acids, and to digestion must therefore be considered the active principal. Finally it has been pointed out by Ford [23] that this hæmolytic substance is frequently present only in small amounts in *Amanita phalloides* and may be absent altogether, while certain edible fungi, *Amanita solitaria* and *Amanita rubescens* contain it in great abundance. The hæmolytic glucoside, therefore, when introduced into the stomach, is certainly harmless and is probably utilized as food.

Treatment.—No definite line of treatment can be recommended in *Amanita phalloides* intoxication beyond that adopted for poisoning in general. The thorough emptying of the stomach and intestines is usually brought about in the natural development of the intoxication and should be encouraged rather than checked. Large quantities of morphia or some other anodyne are indicated to relieve the suffering and pain. The excessive thirst should be checked by the administration of any liquids which can be borne by the irritated stomach and infusions of salt solution, the so-called "artificial serum" of the French may be introduced subcutaneously. No drug has any antidotal effect upon the *Amanita-toxin,* and the only hope of successful treatment lies in the attempt to develop curative antitoxic sera, a procedure which Ford (l. c.) has shown to be theoretically possible.

Poisoning by Amanita Muscaria.

The *Amanita muscaria,* known as the "fly agaric," from the use of its decoction as a fly poison (the "Fliegenpilze" or "Fliegenschwamm" of the Germans) and called in France the "fausse oronge," because of its resemblance to an edible fungus known as the "oronge vraie" (*Amanita aurantioca* resembling, if not identical, with a small *Amanita cæsaria*) is a beautiful mushroom, probably more generally recognized as a poisonous species than is the "deadly Amanita." This is possibly due to its very marked appearance, easily distinguishing it from all other species except the "oronge vraie" (*A. aurantioca*) or to its very bitter taste. Poisoning from its ingestion is by no means uncommon, but the mortality is low, many of the affected individuals recovering without untoward symptoms. Typical specimens of the fungus are very large growing to a height of six to eight inches, with a widely expanded pileus. There is no distinct poison cup, the stem terminating in an expanded bulbous extremity. The stalk is covered with fairly adherent scales which also lie thickly studded on the upper surface of the pileus. The stalk, the under surface of the pileus, the gills and spores are white, although occasionally a few flakes of yellow appear on the stem. The top of the pileus is a beautiful yellowish or reddish-brown in color. This color varies much in different countries. In Italy and France, judging from illustrations, it tends to be a reddish-brown, while in this country it has more of a yellowish tinge. While typical plants are easy to recognize the small or dwarf forms are far more difficult. These forms have few or no flakes or scales in the pileus, the color of which is more decidedly yellowish. In consequence they resemble to a very considerable extent the small or depauperate forms of *Amanita cæsaria.* The fully developed *Amanita cæsaria* is easily recognized by its large size by the smoothness of the pileus, and especially by its development from a universal cup, on the bursting of which the pileus appears not unlike the yolk of an egg surrounded by the white. Finally the color of the *Amanita cæsaria* in typical specimens is far more reddish-brown than that of the *Amanita muscaria.* The chief errors arise either from complete ignorance of the identity and the properties of fungi or from the recognition of the "muscaria" as the "cæsaria" by foreigners. These mistakes may arise in part from certain variations in color shown by the species in different countries. The *Amanita muscaria,* for instance, in some regions of France and Italy has a reddish tinge and the "cæsaria" a yellowish, while in this country the reverse holds true. The "fly agaric" is very abundant in the United States but seems to be somewhat more limited in its distribution than is the "deadly amanita." I have frequently found it in association with the latter in the regions already mentioned, and it is very common in the low-lying, well-matured tracts of land in the vicinity of Baltimore. Cases of poisoning from this fungus are rather rare here, but fatalities have been reported by Forster (l. c.), Cagliéri,[24] and Prentiss.[25] There are many isolated cases reported in the French and German literature, among which may be mentioned those of Orfila,[26] Mautner,[27] Paulet,[28] as well as those collected by Gillot (l. c.)

The symptoms of poisoning are quite distinctive. They appear soon after the ingestion of the fungus, at times almost immediately and frequently within an hour or two. They consist of vomiting, diarrhœa, severe headache, with ocular symptoms (contraction of the pupils, etc.) followed by delirium, a rapid loss of consciousness and terminating in convulsions of the most violent character. Death may result from the intoxication but in the majority of instances, only small bits of the fungus are consumed, owing to their very bitter taste and the effect of the poison gradually wears off. The delirium may be very marked and is followed occasionally by amnesia.

In the cases which recover, the serious symptoms ameliorate rapidly and the period of convalescence once established is short usually, but two or three days. Occasionally fungi either closely related to *Amanita muscaria* or identical with

it lack the bitter principle of the true "muscaria," and are eaten in large quantity with a rapidly fatal outcome.

The poisoning of the Count de Vecchi and his physician in Washington represent an extreme case of this variety of intoxication, and the details are so interesting that the main facts of the excellent report of Prentiss (l. c.) may be repeated. The Count de Vecchi, an attaché of the Italian legation in Washington, considered something of an expert upon fungi, purchased on the street near one of the markets in that city a quantity of mushrooms, recognized by him as an edible species. The plants were collected in Virginia, about seven miles from the city of Washington, and were probably identified by de Vecchi as *Amanita cæsaria*. At breakfast the following morning the Count and his physician, Dr. K., ate the cooked fungi in considerable quantity, noticing their agreeable and even delicious flavor. The breakfast was finished at half after eight, and within fifteen minutes the Count felt symptoms of serious illness. At nine o'clock he was found by his family lying prostrate on his bed and oppressed by the fear of impending death. He developed blindness, trismus, difficulty in swallowing, and shortly lost consciousness. Terrific convulsions then supervened, of such a violent character as to break the bed upon which he was placed. Despite the administration of apomorphia and atropine the Count never recovered from his coma and died on the second day.

The Count's physician, on returning to his office, immediately after breakfast, soon began to be dizzy and to suffer from double vision and other ocular symptoms. He quickly lapsed into unconsciousness, in which state he remained for five hours, with one or two intervals of lucidity. Under treatment with apomorphia and atropine complete recovery set in about seven o'clock in the evening. These two cases represent the extremes of "muscaria" intoxication; on the one hand the profound depression of the nerve centers, resulting in death within 48 hours, and on the other hand the rapid amelioration of symptoms without permanent lesions.

The *active principle* of *Amanita muscaria* is *muscarine*, a chemical substance with the formula $C_5H_{15}NO_3$ and probably an alkaloid. It was first isolated from *Amanita muscaria* by Schmiedeberg and Koppe,[29] and was found to produce experimentally most of the symptoms of *Amanita muscaria* intoxication. Muscarine was later prepared synthetically by the oxidation of choline, but the artificial product is easily decomposed and seldom has the same physiological action that natural muscarine exhibits. As a logical consequence of the knowledge gained of the properties of muscarine, atropine was suggested as a physiological antidote and it has been used with a considerable amount of success.

That muscarine is not the only poisonous principle in *Amanita muscaria* appears from the work of Harmsen[30] who has shown that atropine does not completely neutralize the effect of injections of *Amanita muscaria* in animals. Support is given the contention of Harmsen by the cases reported by Cagliéri (l. c.). Three children, aged 5, 8, and 10 years, ate small quantities of *Amanita muscaria;* nervous symptoms developed almost at once, consisting of restlessness, contracted and then dilated pupils, Cheyne-Stokes respiration, spasm of the muscles of the lower jaw, convulsions, and coma. Despite the liberal use of atropine all three children died within 30 hours. The parents and another child who also had partaken of the fungi, developed the usual symptoms of muscarine intoxication but recovered.

Finally mention should be made of the practice indulged in by peasants of the Caucasus, who prepare an intoxicating beverage from *Amanita muscaria* from which a horrible kind of delirium results. Apparently a certain amount of toleration for the drug develops from its habitual use, although death from a drunken orgie produced by *Amanita muscaria* is not uncommon. Indeed one of the members of the ruling family in Russia is said to have lost his life in this way.

The claim made by McIlvaine (l. c.) that atropine was first used as an antidote for poisonous mushrooms by a physician in Shenandoah, Pa., is not established by an examination of the earlier literature. Schmiedeberg and Koppe (l. c.) in their earliest publications on muscarine suggested the use of atropine in mushroom intoxication and Lauder Brunton in 1874 (Brit. Med. Jour., 1874, Vol. II, p. 617) recommended it for the same purpose. Furthermore, in the cases cited by McIlvaine the fungi eaten were *Amanita phalloides*, upon the effects of which atropine has no neutralizing action, and two of the patients died.

Poisoning by Amanita Pantherina.

Gillot (l. c.) has collected 30 cases of poisoning by *Amanita pantherina*, but the intoxication is not serious and in but two instances did death result. Cases have also been reported by Faure (l. c.) and by Louriot.[31] The symptoms are apparently due to the action upon the nerve centers of the muscarine which the fungus contains (Kobert[32]). The patients begin to show signs of intoxication within a few hours after eating the mushrooms, suffering from the usual gastro-intestinal disturbances. These are accompanied by great excitement, delirium, convulsive seizures, and a peculiar drunkenness not unlike that described in muscarine intoxication among the Koraks. Ocular symptoms, loss of memory, and syncope are frequently seen. Inoke[33] has reported an interesting series of 32 cases of poisoning from the Japanese variety of *Amanita pantherina*. There was but one fatality among these patients; the sufferer showed peculiar nervous manifestations in addition to vomiting and diarrhœa. Dilatation of the pupils, various hallucinations, the sensation of insects crawling over the skin, visions of reptiles and of beautifully colored snakes—red, yellow and brown—were the most prominent symptoms of the intoxication. The feeling of "bien-être," expressed by singing and laughing was common to all the victims. The patients usually made a rapid recovery, but occasionally the convalescence was prolonged over a period of a fortnight.

From this Japanese *Amanita pantherina*, Inoke[34] has isolated choline and muscarine. He states that in Japan this species is used as a fly-poison, replacing the *Amanita muscaria* (Fliegenpilz), which is rare in Japan and devoid of any special toxic action on flies. *Amanita pantherina* is a yellow-topped fungus which resembles the "fly agaric" in many of its essential characters. It seldom grows in the United States, and Atkinson[35] says that

the species known in this country as *Amanita frostiana* (Peck) closely resembles specimens of *Amanita pantherina* received from Bresadola of Austro-Hungary. No cases of intoxication from this fungus have occurred in America.

Poisoning by Morells or Helvellas.

According to Kobert [36] there are no authentic cases of poisoning from the true Morells, of which he recognizes five different species. There are, however, over 160 cases recorded of poisoning from the false Morells, properly called Lorchells, of which the most important species is *Helvella* or *Gyromytra esculenta*. This should properly be called *Lorchella esculenta*. Its active principle was isolated by Boehm and Külz,[37] who named it Helvellic acid. It is a hæmolytic substance, acid in reaction, with the empirical formula $C_{12}H_{20}O_7$. It had previously been shown by Boström,[38] and Ponfick,[39] that the poisonous principles in *Helvella esculenta* were completely soluble in hot water, the aqueous extract killing dogs when given by stomach, while the residue left after extraction was quite harmless. The symptoms of intoxication in these animals were the same as when the fresh fungus was fed them, and in both intoxications there was marked hæmoglobinuria pointing to a hæmolytic poison. According to both Boström and Ponfick the toxicity of *Helvella esculenta* disappears or is much lessened when the fungi are dried. Helvellic acid, as obtained by Boehm and Külz is also toxic to dogs when given by mouth, likewise producing hæmoglobinuria, and there can be no doubt that it is the active principle. The Morells are eaten to some extent in the United States, but no cases are on record where the poisonous *Helvella esculenta* was mistaken for them.

Poisoning from Other Varieties of Fungi.

In addition to the species already described the lethal effects of which are well established, a number of other fungi are credited with poisonous properties, and rarely death has been ascribed to their ingestion. In many of these cases, as in poisoning from *Russula emetica*, the symptoms point to the presence of muscarine in the fungus, together with substances producing a profound gastro-intestinal disturbance. Such fungi have usually a bitter, disagreeable taste and are strongly emetic. In consequence, but small amounts of the plants are eaten, and the violent retching produced soon rids the system of the offending morsels. Certain species of *Phalloideæ* are eaten greedily by animals, especially by swine, with disastrous effects. These plants exhale a very offensive odor and are probably never eaten by man. In Gillot's collection of cases several deaths are traced to the *Volvaria*, but little or nothing is known of the active principle. Finally the *Boletus satanus*, which is believed to be poisonous, is known to contain muscarine.

No cases of poisoning have ever resulted from the use of any of the purple-spored or black-spored agarics.

These plants, like many other foods when slightly decomposed, may give rise to severe intestinal disturbances, with marked prostration. The cases of poisoning reported from the field or meadow mushroom are not authentic. In the majority of instances the fungi said to be *Agaricus campestris* were not identified as such by competent authorities, and where any description of the plants has been given it is apparent that either *Amanita phalloides* or *Amanita muscaria* was eaten by mistake for the ordinary mushrooms. Many fatal cases of "toadstool poisoning" are reported in both medical and lay journals, without any statements as to the fungus eaten. The course of the intoxication and the post-mortem findings point invariably to the consumption of such well-known species as the "deadly amanita" or the "fly agaric." Indeed, in the vast majority of such fatal cases reported, both in this country and in Europe, I am convinced from a careful study of the symptoms that *Amanita phalloides* is the offending species.

Collectors of mushrooms should limit themselves to the use of well-known species, such as the purple and black-spored Agarics, the edible species of Boletus and certain varieties of Lactarius and Polyporus. White-spored Agarics should always be avoided even if the edible *Amanita cæsaria* or *aurantioca* is thus lost to the pleasure-loving palate. Especially should the *Lepiota* and the *Amanitopsis*, species closely to *Amanita phalloides* be strictly eschewed. While the typical plants, perhaps, are not difficult to identify, specimens of *Amanita phalloides* in which the veil has dropped off closely resemble the *Amanitopsis*, and those in which the poison cup is sunk deep in the ground may readily be mistaken for *Lepiotas*. For an excellent list of edible and poisonous mushrooms those interested in this phase of the subject should consult the last edition of Kobert's Lehrbuch der Intoxikationen.

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of Boletus and to unknown fungi. The other 4 deaths showed symptoms of *Amanita phalloides* intoxication. He reports 44 additional cases with 14 deaths, including those already reported by Trask (l. c.). Of these cases 26 had symptoms of *Amanita phalloides* intoxication. Of the 14 deaths 7 were due to *Amanita phalloides*, 2 probably to *Amanita muscaria*, while the others were of unknown origin.

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A REVIEW OF ONE HUNDRED AND FIVE REPORTED CASES OF ACUTE PANCREATITIS, WITH SPECIAL REFERENCE TO ETIOLOGY; WITH REPORT OF TWO CASES.

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The following work was undertaken primarily for the purpose of obtaining an idea as to the relative frequency of the different causes of acute pancreatitis, but in going over the cases other conditions of interest were noted which will be referred to in their place. The studies of Langerhans, Robson, Koerte, Flexner, Bloodgood, Opie, Halsted, and others are so well known that it is hardly necessary to mention them except to make brief references in presenting the present status of the subject.

Bloodgood divides acute pancreatitis clinically into two groups, the first characterized by exudate of serum and blood into the pancreas and peripancreatic tissues usually associated with disseminated fat necrosis and intraperitoneal hæmorrhagic exudate. The second group is characterized by suppuration and formation of one or more abscesses; usually there is more or less gangrene of the pancreas present. He says pathologically, undoubtedly every case of pancreatic abscess passes through the first stage of the disease.

Etiology.—Many causes have been given as etiological factors in the production of acute pancreatitis. Besides gallstones causing retrojection of bile into the pancreas we have injury and various infections given as probable causes. In cases of retrojection of bile and injury the various organisms as *B. coli communis*, the pyogenic organisms and a number of less common bacteria are frequently met with as secondary invaders, and it seems probable that the more often they are looked for the more frequently they may be found. When we consider the frequency with which bacteria are found in the bile, and the ease with which the pancreas can be infected, due to its position, we can readily see how infection may occur simultaneously with the retrojection of bile or immediately after. In the same way, in the case of injury, a condition favorable for the entrance of bacteria is established, and infection results.

In those cases in which mechanical conditions, as gallstones or pancreatic calculi, are not the primary cause various conditions may bring about infection. Gastro-duodenal catarrh, especially the alcoholic form, is mentioned by many authors as existing in cases of acute pancreatitis.

The bacterial invasion may be from the intestine through the ampulla of Vater and the pancreatic ducts or, in cases where the bile contains organisms, from the common bile ducts into the duct of Wirsung. Another method of invasion in cases of duodenitis is by direct extension through the wall of the intestines into the head of the pancreas. It is impossible to say how often these different methods of infection occur in a given number of cases. Robson says infection through the ducts is the most common. Infection may take place through the blood-stream or the lymphatic system, but here again we are in the dark as to the relative frequency of infection through these avenues. There is a group of cases in which the method of infection cannot be established—no gall-stones

are present, no inflammatory lesions, and the person has been in apparently perfect health. It would be interesting to know the condition of the bile in these cases and what diseases these patients had had during their lives. When we consider that *B. typhosus, B. coli communis* and some of the pyogenic bacteria may live for months and years in the bile it seems not at all improbable that many of these cases may have their source of infection in the gall-bladder. Another possible cause are emboli leading to infarction of portions of the pancreas. Munzer believes giant cells from the placenta may become emboli and cause necrosis of the pancreas.

The pancreatic ferments have been supposed to be able to produce pancreatitis, as Chiari has noticed autodigestion of the pancreas accompanied by multiple small hæmorrhages shortly before death, but, as Pearce states, there is no definite proof that true hæmorrhagic pancreatitis is ever produced by this cause.

Hlava believes that gastric juice may be forced back through the ampulla of Vater by antiperistaltic action of the intestines, and that it may be a cause of pancreatitis, but Pearce has shown experimentally, that under normal conditions this cannot take place; all of his experiments being negative. In going over the published cases of pancreatitis one case of chronic pancreatitis was found in which the gastric juice was supposed to be the cause of the condition, but in this case, a gastro-pancreatic fistula was present through which the gastric juice had gained access to the pancreas, producing a chronic interstitial pancreatitis and not an acute pancreatitis. However, experimentally acute pancreatitis has been produced by Flexner by the injection of artificial gastric juice.

Robson says, that owing to the soft character of the gland tissue, an auto-destructive ferment, which dissolves the wall of the blood-vessels and produces a hæmorrhage, is set free by any injury to the pancreas however it may be inflicted.

Carnot, on the basis of a large number of experiments, concluded that the intensity of tissue alterations was more a cause of gland changes than the nature of the exciting agent. He says further, the more acute the symptoms the greater the liability to hæmorrhage which may follow traumatism as well as poisoning by mercury and other chemicals.

Wiener says, "We know that we frequently find infections of the gall-bladder and ducts without the presence of stones. May not such an infection cause so great a swelling of the mucous membrane of the common duct that the papilla of Vater is occluded? We certainly believe that it may."

Robson thinks the causes of diseases of the pancreas are the same as those of the gall-bladder. A reason why the pancreas is less often affected than the gall-bladder, as Truehart states, may be due to the bactericidal property of the pancreatic secretion.

Pearce says there are four possibilities as to the means by which hæmorrhagic pancreatitis is produced in man. 1. Action of ferments originating in the pancreas. 2. Bacteria. 3. Gastric juice. 4. Bile. In regard to the effect of blood on the pancreatic tissues Hart states that this effect is not seen if the corpuscles are removed.

Lancereux states that pancreatic affections are due to a nervous agency or infection. In one of the cases mentioned by Fitz in his Middleton-Goldsmith lectures, Osler and Hodges found round-cell infiltration in the solar plexus.

Deaver says he believes that cases of sudden onset and rapid course will be found to be due in most cases to gall-stones in the ampulla or immediate vicinity; and cases more gradual in onset due to infectious inflammations about the ampulla.

Fat necroses.—This was first described by Balser in 1882; and Fitz in 1889 pointed out the relation between pancreatitis and fat necrosis. The first to show the relation between fat necrosis and steapsin were Langerhans and Flexner. The fat splitting ferment coming in contact with fat, splits this into fatty acids and glycerine. The glycerine is absorbed, while the fatty acids combine with calcium salts to form soap. The basis for Cammidges reaction is the appearance of the absorbed glycerine in the urine. This glycerine aside from jaundice is also supposed to be a cause of the hæmorrhagic tendency seen in various pancreatic diseases. Cammidge produced hæmaturia and hæmoglobinuria rapidly in urine by injecting very small amounts of glycerine. In two cases there was a striking diminution in blood platelets compared with normal blood. Opie makes the following statements in regard to fat necrosis. 1. The condition essential to the production of focal fat necrosis is the penetration of the fat-splitting ferment of the pancreas into living adipose tissue. 2. By causing the entire secretion of the pancreas in cat to penetrate into the tissue surrounding the organ, wide diffussion takes place and necrosis results, not only in the abdominal fat but in that of the pericardium and subcutaneous tissue as well, thus reproducing the widespread distribution of the lesion occasionally observed in man and in lower animals. 3. Lesions of the pancreas associated with focal fat necrosis are such as permit the diffusion of the pancreatic ferment into the surrounding tissue.

According to Flexner, the pancreatic secretion may enter the abdominal cavity without causing diffuse inflammation. Woolsey quotes Ceccherelli as saying that extravasation of normal pancreatic secretion into the peritoneal cavity never causes peritonitis.

Glycosuria.—Robson says Körte found glycosuria in two out of forty-one cases of hæmorrhagic and in three out of forty cases of gangrenous pancreatitis. In his own experience glycosuria is a very rare phenomenon. It occurs only when there is great destruction of tissue as in extensive cirrhosis or malignant disease. Fat and indigested muscle fibers in stools is more common; lipuria is not as common. These conditions occur too seldom to be of much use in diagnosis, but when they do occur they are of great importance. According to Dieckhoff, an analysis of fifty-three cases of pancreatic disease in which diabetes occurred, showed that 10 per cent of them were due to pancreatitis.

The following cases were chosen from the available cases,

most of which have been reported within the last few years. Only those were chosen in which the etiology was stated or in which it was possible to point out the probable cause. No attempt has been made to pick out any particular class of cases.

Cases in which Gall-Stones were Present, or Believed to be Present.

In this series there are forty-four cases. In three the stone was in or near the ampulla of Vater, and may possibly have caused the retrojection of bile into the pancreas. Opie has demonstrated how a stone in the ampulla may cause retrojection of bile, and Halsted has shown the necessary conditions in order that this may take place. Flexner has, in a recent article, published experimental results, proving that the bile salts are the agents by which an acute pancreatitis is set up; the nucleo-albumin of the bile, a colloidal substance, has a restraining action on these salts.

Associated infections.—The most common organism associated with gall-stones in this series was *B. coli communis.* It was present alone in one case. It was associated with *S. pyogenes* and *M. pyogenes aureus* in one case. In the latter, *B. coli communis* was found in the liver and kidney; the two others were found in the peritoneal cavity. In another it was associated with the *B. lactis ærogenes* and *B. proteus vulgaris,* the three being present in and around the pancreas. In two other cases bacteria were present but not identified. In one a short bacillus was found in the duct of Wirsung. In the other bacteria were found in the mass at the location of the pancreas. In one case the gas bacillus was probably present.

Strangulated hernia.—One patient had a strangulated inguinal hernia. The onset was with severe pain in the lower part of the abdomen. It is difficult to say whether the pancreatitis in this case was due to gall-stones or the gastro-intestinal disorder following the strangulation.

Abnormalities.—In New's case gall-stones were present but the duct of Wirsung had a separate opening. Although it would be impossible for bile to be forced back an inflammatory process might spread either from the gall-ducts or from the intestines. The patient suffered from nausea and vomiting and was indisposed before the onset of the severe pain indicating pancreatic involvement, she had also suffered from constipation. These points would indicate gastro-intestinal disorder of some kind which, in connection with the general jaundice present, makes it possible that the infection was from the intestines in this case.

In Polkoff's patient the history pointed to gall-stones and was associated with glycosuria. In a case reported by Pearce the duodenal papilla, common duct, and pancreatic duct were dilated, making it very probable that a gall-stone had been present. A marked alcoholic history and duodenitis were also present in this case. Two other cases had had typhoid fever, were over 40 years of age, and both were women. In the remaining no predisposing factor to gall-stones can be pointed out. The cases reported by Trafoyer and Chiari are of special interest for the reason that the pancreas was passed per rectum in both patients.

Pancreatitis Due to Other Causes than Gall-Stones.

In looking over the reported cases of acute pancreatitis one is at once impressed with the fact that in a considerable number of cases gall-stones cannot be found, and therefore one must look for some other etiological factor to explain the disease. It is very difficult without the most painstaking search to say exactly what the cause is in a given case belonging to this group, and sometimes it is impossible. In the first place it is necessary to exclude gall-stones. A very small stone, as, for example, in Opie's first case, may suffice to cause the attack and can be easily overlooked, especially if the intestines are not carefully examined. In one of Thayer's cases the stone was found in the intestines.

In the second place, a careful bacteriological examination made under favorable conditions is necessary. In a considerable number the *B. coli communis* is found in the pancreas. Is this organism the exciting cause or is it a post-mortem invader? A number of very able investigators believe the latter to be true in the majority of cases. Another difficulty is to explain exactly the method of infection. Only a careful, systematic examination at autopsy will be able to show the relative frequency of the different conditions bringing about pancreatitis in this particular group.

A large number of these cases are preceded by gastro-intestinal disorders ranging from a feeling of heaviness to pain and attacks of nausea and vomiting, and in fact, it seems to me, judging from this series, that relatively the most common condition present which can be said to be a causative agent is gastro-duodenitis. This is especially true when the alcoholic cases are included, as it is supposed alcohol predisposes to pancreatitis by causing a gastro-duodenitis.

In this series thirty-two had a preceding history of gastro-intestinal disorder, in which it is possible to point to this as the probable cause.

In Germain and Christian's patient a careful study was made to determine the possible method of infection. The case is unique in that it was an early stage showing inflammation but no hæmorrhage. The authors suggest that the duodenitis was the primary lesion and that the inflammation spread by direct extension through the intestinal wall, or through the ducts.

Summarizing these cases we have the following results:

Total number with preceding or associated gastro-intestinal disturbances, 32 cases.

Gastro-duodenitis due to alcohol or in which there is a history of alcoholism, 17 cases.

Gastro-duodenitis in which there is no history of alcoholism, 15 cases.

Gastro-duodenitis not due to alcohol associated with *B. coli communis,* 1 case.

Alcoholic gastro-duodenitis associated with *B. coli communis*, 1 case.

Gastro-duodenitis not due to alcohol associated with bacterial infection, of indefinite nature, 1 case.

Acute Pancreatitis Following other Conditions than Gall-Stones and Gastro-Intestinal Disturbances.

Appendicitis.—It is impossible to state definitely the manner of infection in these two cases. It may have been through the circulatory system or by direct extension. In one the intestines were found markedly congested.

Typhoid fever.—Chauffard and Revant report a case of typhoid fever from which the patient had practically recovered when he was suddenly seized with a fatal attack of pancreatitis from which he died sixty-six days after the onset.

Moynihan's case was, strictly speaking, of a chronic type. The patient had an attack of typhoid fever about a year and a half before an operation from which he had recovered. Typhoid bacilli were demonstrated in the bile which showed the nature of the pancreatic disturbance. In this case there had been repeated inflammatory disturbances in the pancreas. When the relative frequency with which the parotid gland is involved in typhoid fever is recalled it seems rather strange why the pancreas is no more frequently attacked especially when the ease with which the infection may take place is recalled.

Mumps.—Simonin reports ten cases of pancreatitis occurring in 652 cases of mumps treated at the Hospital of Valde-Grace. It is worthy of notice that in one case the onset was with violent epigastric pains, followed the day after by parotitis. One case was complicated by an epididymitis; three cases by orchitis. All recovered. Simonin says the pancreatitis in these cases was probably of the nature of an œdematous interstitial infiltration of the soft gland tissue, comparable to that seen in the parotid. Zeller reports one case similar to Simonin's series.

Boils.—Porter's patient had typhoid fever one year before and suffered with frequent attacks of quinsy, and had been troubled with boils for four or five weeks before present illness, the probable cause being an infection from the boils.

Malaria.—According to Ross and Daniells pain was not a notable symptom in this case. That the malarial parasite will cause extensive thrombi in the smaller blood-vessels of the stomach, intestines and elsewhere has been demonstrated by Machiafava and Barker.

Gastric ulcer.—One case.

Duodenal perforation.—One case.

Oxalic acid.—This is really a case of unknown etiology. The patient had taken oxalic acid, but had apparently recovered and left the hospital to return two days later with marked bronchial symptoms. The author, Frederick Taylor, suggests that the oxalic acid poisoning masked the pancreatic disturbances.

Emboli.—Two cases, both died. Reported by Kraft.

One of these patients had suffered for some time with heart disease. During the last illness the patient had symptoms of abdominal disorder and at autopsy infarctions in the pancreas were found leading to a condition of acute hæmorrhagic pancreatitis.

Syphilis—This case Kraft believes was due to a syphilitic process in the pancreas. The patient used alcohol to excess.

Bronchitis and cardiac disease.—This patient never had symptoms of abdominal disturbance. Kraft, in connection with this case, makes the statement that he believes it is possible for an acute pancreatitis to follow a severe disease without manifesting itself in symptoms, just as a parotitis may follow a septicæmia or certain other diseases without producing symptoms.

Pulmonary tuberculosis.—One case; reported by Kraft.

Retrojection of bile from cause unknown.—The common duct, duct of Wirsung, and pancreas were bile-stained. The patient had for two days before the onset of the disease slight abdominal pain which might have been a duodenitis and a possible cause of the retrojection of bile in view of the absence of gall-stones and pancreatic calculi. In this case on microscopical examination a very small carcinoma was found in the pancreas, but it was believed by Sappington, who reports the case, not to be in any way associated with the pancreatitis.

Possible trauma.—Three cases, all recovered. Jones' patient was seized with severe epigastric pain on turning in bed. That pancreatitis will follow very slight injuries is known. Moynihan speaks of an attack following a very slight blow on the abdomen. In this case a pancreatitis of the hæmorrhagic type developed ending in death.

SUMMARY.

Acute pancreatitis	following	gall-stones or suspected gall-stones	.....	44
"	"	"	gastro-intestinal disturbances..	32
"	"	"	typhoid	2
"	"	"	or associated with appendicitis.	2
"	"	"	duodenal perforation.....	1
"	"	"	drinking of oxalic acid.....	1
"	"	"	gastric ulcer.....	1
"	"	"	boils	1
"	"	"	emboli	2
"	"	"	malaria	1
"	"	"	syphilis	1
"	"	"	trauma	3
"	"	"	bronchitis and heart disease...	1
"	"	"	pulmonary tuberculosis.....	1
"	"	"	retrojection of bile from unknown cause	1
"	"	"	mumps	11

Onset.—It has been supposed that in cases of acute pancreatitis due to gall-stones that the onset, as a rule, is more sudden than in the cases brought on by other conditions, but in this series the discrepancy is so slight as to make no practical difference. In this series the onset in those due to gall-stones or supposed to be gall-stones, was sudden in forty-one out of forty-four cases. In those preceded by gastro-intestinal disturbances the onset was sudden in twenty-seven

out of thirty-two. Sudden onset was also the rule in most of the cases following miscellaneous causes. It will be seen on looking over the symptoms of onset, how closely they in general correspond to the original description of the onset given by Fitz.

Mortality.—Of the forty-four cases associated with gall-stones thirty died. Of the thirty-two associated with gastro-intestinal disturbances seventeen died, a considerably better showing than in the gall-stone cases.

Of the remaining cases following miscellaneous causes one associated with typhoid fever recovered and one died. One appendicitis case recovered and one died. The three cases following traumatism, the eleven cases following mumps, and the one following gastric ulcer recovered. The others died. It should be remembered, however, that in the latter group there are cases that had fatal diseases preceding the pancreatitis.

Sugar was present in the urine in six cases. Three of these were associated with gall-stones, one with retrojection of bile from cause unknown, the fifth was associated with gastro-intestinal disorders, and the sixth with gastric ulcer. Three recovered and two died. In regard to one there is no statement as to recovery. The two that died both were possibly associated with retrojection of bile, in one there was definite evidence of bile in the duct of Wirsung, in the other gall-stones were present, and in addition typhoid fever. Sugar is supposed to be present in the urine in cases of pancreatitis only when there is great destruction of pancreatic tissue. In one case, the islands of Langerhans were unaffected; in another gangrene had set in in certain areas.

Complications.—Pneumonia occurred in three cases. Insanity of several years' duration was present in one case, the pancreatitis being the cause of death. Enlargement of the parotid gland was seen in one case. Delirium tremens was present in one case that ended fatally. The delirium had apparently come on shortly before or simultaneously with the pancreatitis. Epididymitis was seen in one case, and orchitis in three of the cases of pancreatitis following mumps. In Sappington's case a small carcinoma was found on microscopical examination.

Fat necrosis was present in nearly all the cases operated on, or seen at autopsy. These necrotic areas were found not only in the abdominal cavity but also on the pericardium and in the subcutaneous fat. Moynihan mentions a case of Hanseman's where bright red spots occurred on the skin over underlying foci of necrosis in the subcutaneous abdominal fat.

Kraft explains the symptoms seen in pancreatitis on the basis of Lennander's findings in regard to the sensibility of the peritoneum. Lennander has shown that the parietal peritoneum is very sensitive, especially the diaphragmatic portion; and that the portion covering the viscera, colon, mesentery, and liver is not as sensitive. Kraft says the pains begin with the hæmorrhage which causes a stretching of the pancreatic capsule and of the retro-peritoneal portion of the peritoneum in the saccus epiploicus. If the stretching remains stationary for some time the peritoneum adapts itself to the pressure and the pain lessens or disappears to recur again with any new hæmorrhage. At times the hæmorrhage extends down along the mesocolon of the ascending and transverse colon; in these cases there will be pain in the right side of the abdomen.

Kraft has endeavored to point out the different routes that a pancreatic inflammation may take in spreading. Most frequently the inflammation spreads over the peritoneum of the saccus epiploicus closing the foramen of Winslow, thus preventing further extension. If the inflammation spreads through the foramen of Winslow it will spread between the transverse colon and the liver, causing tenderness along the curvature. The inflammatory process will spread further along the ascending colon and finally it may enter the larger peritoneal cavity at the cæcum. Only on rare occasions will the inflammatory process follow the same route as the hæmorrhage. If the hæmorrhage has spread down into the mesocolon, ascending tenderness over McBurney's point may be present and cause some confusion in diagnosis.

Doberauer and Guleke have both recently published papers showing that absorbed trypsin is the cause of the marked collapse and death in pancreatitis, especially in the acute form.

I wish to report briefly two cases that have come to my notice. For notes on Case 1 and for the pancreatic specimen I am indebted to Dr. Sams, of Clarion, Ia.

Case 1.—Male, age 36 years. Family history, negative, except for history of tuberculosis in sister. Past history: always well. Present illness.—The patient ate a hearty Christmas dinner; did not feel well for several days following. On January 6, 1906, he became worse. He was seized with colicky pains in epigastrium, became nauseated, was markedly constipated; showed signs of collapse, had some hiccough.

Examination.—No tympanites; slight tenderness in epigastric region. Pulse rapid; temperature normal; urine negative. His physician made a diagnosis of acute pancreatitis.

The patient died January 29, thirty-five days after the onset of illness, and twenty-three days after the onset of symptoms pointing to pancreatitis.

Post-mortem.—Heart and lungs negative, except for a nodule in the apex of right lung. Left rectus muscle black in color. No peritoneal fluid, no abdominal adhesions; appendix normal; liver enlarged; gall-bladder distended with tarry bile; no stones, common and cystic ducts enlarged and thickened. Stomach and duodenum showed marked evidence of chronic catarrhal inflammation, most marked at pyloric end of stomach.

Pancreas.—Head of pancreas considerably enlarged; body and tail not much enlarged. Whole organ is dark in color and in places black. A number of areas of fat necrosis present. On section the cut surfaces present a mottled black and gray color; the greater portion of the organ being dark in color and

in a few places black. The duct of Wirsung is bile stained, the stained portion extending back into the organ about 1 cm.

Microscopical examination.—All sections examined showed a great number of hæmorrhagic areas, and considerable necrosis of gland tissue. The sections from the head of the gland showed some connective tissue proliferation. Islands of Langerhans had disappeared in some of the sections, in most of the sections they were intact. A few needle-shaped crystals were seen in preparations made from areas of fat necrosis. Every section examined showed areas of necrosis and inflammation. A few cocci and short bacilli present.

Anatomical diagnosis.—Acute hæmorrhagic pancreatitis.

In this case the primary lesion was probably in the stomach and intestines. As there was evidence of bile having been forced back into the pancreas, in view of the absence of gall-stones at autopsy it seems that the ampulla of Vater may have been closed by the gastro-duodenal catarrh present. The infection may have spread from the intestine by any of the routes already mentioned. The thickened biliary ducts and the connective tissue proliferation in the head of the pancreas would indicate that gall-stones may have been present at some time or other.

For notes on Case II, I am indebted to Prof. Jepson and Dr. Burge.

Case II.—Female, age 27 years, married. Admitted to the surgical side of the University Hospital, May 10, 1904. Family history, negative. Past history: The patient has had some stomach trouble for past seven years, otherwise has enjoyed good health. About one year before present illness she had been confined in child-birth. Eight weeks ago (early in January, 1904), she had an attack of typhoid fever. Six weeks after onset severe stomach trouble set in with epigastric pain, nausea, and vomiting; on several occasions blood was seen in vomitus. She grew steadily worse.

Examination.—Moderate distention of abdomen with tenderness, especially marked in the epigastric region. A diagnosis of gastric ulcer was made and an exploratory operation was decided on. At the operation, Dr. Jepson found a great amount of pus in the lesser peritoneal cavity, which was evacuated. Patient continued to have a septic fever and later had sugar in the urine and fat in the stools. Her digestion was very poor. Wound closed six weeks after operation. She died eight weeks after the operation, and about four months after the onset of typhoid fever.

Autopsy.—(Dr. Burge.) Cicatricial tissue in numerous areas throughout intestine, showing evidence of healing of ulcers in Peyer's patches. Head and body of pancreas completely destroyed, only a small part of tail of pancreas being left. Grayish necrotic material and pus at site of pancreas. No gall-stones in gall-bladder or ducts, liver normal. No other pathological changes found.

Microscopical examination.—(Dr. Albert.) Marked necrosis of pancreatic tissue. Very few pancreatic cells left; in these the nuclei failed to stain; the contained protoplasm showed numerous granules. No islands of Langerhans were seen and no extravasated blood was present.

Anatomical diagnosis.—Acute suppurative pancreatitis.

In this case, although *B. typhosus* was not isolated from the necrotic material occupying the site of the pancreas the association of pancreatitis with typhoid fever makes the presumption justifiable that it was a case of pancreatitis following typhoid fever.

In five other cases in this series besides those associated directly with typhoid fever there is a previous history of attacks of typhoid fever. No other acute febrile disease occurred so often. Erysipelas and rheumatic fever occurred twice; pneumonia, influenza, malaria and scarlet fever occurred once in separate patients.

The presence of sugar in the urine and of fat in the stools is another point of interest in this case.

Conclusions.—1. Gall-stones are probably the most common single cause of pancreatitis. Judging from this series about forty-two per cent of the cases of acute pancreatitis are associated with gall-stones.

2. Gastro-intestinal disorders are the next most common cause of acute pancreatitis. In this series of cases about thirty per cent belong to this group. Seventeen out of thirty-two of this group gave a history of alcoholism. It is very probable that retrojection of bile may be caused by intestinal disorders closing the papilla of Vater.

3. Acute pancreatitis may be caused by many other conditions. Among these we have typhoid fever, tuberculosis, mumps, trauma, syphilis, emboli, appendicitis, malaria, and gastric ulcer.

4. The organism most commonly present is *B. coli communis;* next comes the streptococcus and the staphylococci.

5. Typhoid fever is the most common of the acute febrile diseases present according to the previous histories of these cases of acute pancreatitis. In the present series three were directly associated with typhoid fever alone, and four had suffered from typhoid fever sometime before the onset of acute pancreatitis, and had apparently recovered; another had had typhoid fever and erysipelas. But two out of these eight cases were associated with gall-stones. It should be kept in mind that in this latitude typhoid is the most common continued febrile disease.

In conclusion I wish to express my thanks to Dr. Bloodgood, of Johns Hopkins University, at whose suggestion this work was undertaken, and who has kindly placed at my disposal his own collection of cases. I wish to thank Dr. Jepson, Dr. Albert, and Dr. Burge, of the State University of Iowa, and Dr. Sams, of Clarion, Iowa, for notes on the two cases reported. To Dr. Decker, assistant in pathology, I am indebted in various ways for help in the preparation of this paper.

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VENA CAVA SUPERIOR RECEIVING TWO UPPER RIGHT PULMONARY VEINS AND OPENING INTO BOTH ATRIA.

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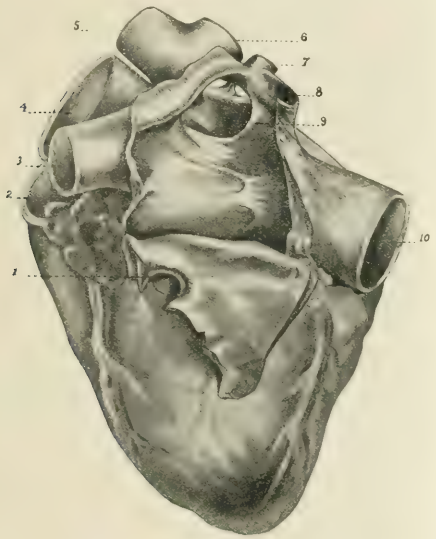
A patient who had died at the Cleveland City Hospital was brought for an autopsy to the Medical College last year. As far as could be learned he had never suffered from his heart. When the post-mortem examination was made the heart was found to present two anomalies, which alone will be described; the rest of the examination showed no other malformations.

The organ is slightly larger than normal, weighing 350 gms., the enlargement being best marked in the right side, although the walls are but little increased in thickness. Both atria seem rather large. The ostium venosum dextrum is wide, measuring 140 mm. in circumference, but the ostium venosum sinistrum is much smaller, measuring but 80 mm. The aorta and arteria pulmonalis seem normal save for atheromatous changes in the former.

On inspecting the heart one's attention is first drawn to the disposition of the vv. pulmonales. On the left side these are two in number, on the right side, however, there are three; of these the inferior opens into the atrium sinistrum high up, close to the v. pulmonalis superior sinistra. The other two veins, vv. pulmonalis superior dextra and media, the latter being very much smaller, open into the v. cava superior, their orifices being less than two mm. apart. The middle pulmonary vein opens at the junction of the vena cava and the atrium.

Upon opening the atrium dextrum, which is capacious and whose musculi pectinati are well developed, nothing abnormal is at first seen. The fossa ovalis is well defined and completely closed in by membrane which is opaque, the valvula Eustachii



Heart Seen from the Left, Below and Behind.

1. Vena pulmonalis inferior sinistra (cut into in forming flap).
2. Arteria pulmonalis.
3. Vena pulmonalis superior sinistra.
4. Aorta ascendens.
5. Vena cava superior.
6. Vena pulmonalis superior dextra.
7. Vena pulmonalis media dextra.
8. Vena pulmonalis inferior dextra (cut into in forming flap).
9. Lower edge defect or upper edge of septum atriorum, just above which can be seen the orifices of the two upper right pulmonary veins on the farther wall of the superior cava.
10. Vena cava inferior.

thick and well developed. The walls of the atrium sinistrum are smooth save for two small folds on its inner wall which may represent the remains of valvulæ foraminis ovalis but which offer no means of communication between the auricles. High up, however, its inner wall is deficient, so that here it connects with the v. cava sup., just where this empties into the atrium dextrum. This defect is limited below by the thick, smooth, deeply concave margin of the septum atriorum; this free edge of the septum blends posteriorly with the wall of the v. cava sup. just below the point of opening of the v. pul. media dext., while its other extremity can be traced on the antero-medial wall of the vessel as far as a point opposite the center of the v. pul. sup. dext. It thus divides the cava into two parts, and as viewed from above, the opening into the atrium sinistrum is slightly larger. This defect has, therefore, no upper limits and the septum atriorum if projected upward would divide the cava almost symmetrically. A line drawn through the v. pul. sup. sin. and the v. pul. media dext. passes several mm. above this free border of the septum. The defect is not readily seen from the atrium dextrum, being situated high up and partly hidden by the crista terminalis, its lower limit being fully 2½ cm. above the fossa ovalis.

In my search through the available literature I have found no similar cases described. Concerning the abnormal emptying of the pulmonary veins I have found little more than a mere enumeration of possibilities, Peacock[1] putting it among the more common venous cardiac anomalies, and Rauber[2] stating it to be very unusual. With very rare exceptions defects of the primary septum are below (Rokitansky[3]) and are usually associated with other malformations. In 62 cases of communication between the atria collected by Deguise in only 17 was it the only abnormality (Vierordt[4]).

Among the cases bearing some resemblance to this are the following:

Peacock.[5] In the museum of St. Thomas Hospital, specimen marked "D. 62 is a preparation of the heart of a child, six years of age, who presented no signs of disease of the heart till she had scarlet fever, 10 weeks before death. An opening, nearly circular in form and six lines in diameter, exists at the upper part of the septum atriorum above the foramen ovale and the latter passage is closed except that a small valvular communication still exists."

Wagstaffe.[6] First case. "On examining the auricular septum after death it was found that a large aperture existed in its upper part, directly below the entrance of the superior vena cava and about an inch in its transverse diameter."

Second case. "An opening nearly circular in form and six lines in diameter exists at the upper part of the septum auricularum, above the foramen ovale, leading as in the previous case directly from one into the other auricle."

Chiari.[7] Heart large, right ventricle enlarged and hypertrophied. In the upper posterior part of the septum atriorum is an opening 15 mm. in diameter. Foramen ovale, open, pea-size; one large and three small right pulmonary veins empty into the right auricle to the right of a line connecting the superior and inferior cava. Abnormal opening of the pulmonary veins is here considered primary, defect secondary, due to excessive amount of blood from both cavæ and right

lung in the right auricle constituting a disturbing factor in the development of the septum.

Hepburn.[8] Three right pulmonary veins open into the superior cava close to the atrium, two into the left atrium, but closely adherent to the wall of the right auricle. Right auricle dilated, foramen ovale closed. "In the septum atriorum an inch above and quite distinct from the upper margin of the fossa ovalis, there was an ovoid foramen forming a communication between the auricles. The short axis of this foramen measured three-eighths of an inch, its long axis was in the line of the superior vena cava, its upper end being close to the posterior margin of the opening into the right auricle, common to the superior vena cava and the upper right pulmonary vein."

Opening of the vena cava inferior (ascendens) into both atria has been recorded by Rokitansky[9] in six cases in conjunction with other defects.

Defects in the lower part of the septum atriorum, near the venous ostia are the most common and readily explained by a reference to their development. (Vierordt,[10] Minot,[11] Kollmann,[12] Hertwig.[13])

The septal defect in this case, or what is rather more descriptive, the opening of the vena cava superior into both atria seems to be due to the development too far to the right of the septum primum (septum superius of His; primäres septum of Rokitansky). So far, indeed, that, instead of passing to the left of the superior cava, it passes directly through the opening of this vessel and encountering here nothing to which it can form attachments a defect must needs result and any tendency toward subsequent closure would be counteracted by the increased amount of blood in the right atrium and indeed in this very locality. Part and parcel of this same defective process would appear the development of the right pulmonary veins. These all empty higher than usual and the upper two farther to the right than normal. It is as if the disturbing factor was in the atrium sinistrum carrying both the septum and the pulmonary veins so far over to the right as to encroach upon the superior cava. That more than the usual amount of the original pulmonary veins on the right side have been taken up into, and become a part of, the wall of the atrium sinistrum in its formation is indicated by their being three in number and not two as is usual, and as is the case on the opposite side, *i. e.*, the process of extension and growth of the atrium sinistrum has progressed far enough to take in and make a part of its walls not only the two right tributaries of the primitive pulmonary vein but in addition the first tributary of one—the upper—of these as well. Thus, in two of the cases quoted above, where the pulmonary veins empty into the superior cava or right auricle they are also increased in number. The development of the septum secundum was apparently undisturbed.

The accompanying illustration shows the condition very well, the heart is represented as viewed from the right, below and behind the atrium sinistrum having been opened.

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October 15, 1906.

Excision of the Sigmoid in a Case of Volvulus. Dr. Bloodgood.

The case presented by Dr. Bloodgood was an example of chronic volvulus of the sigmoid flexure. The giant sigmoid colon had been resected August 16, 1905, followed by a lateral anastomosis. The patient recovered without complications.

It is of interest clinically because this man, now 65 years of age, has been admitted to the surgical clinic during a period of sixteen and a half years, thirty-one times, for attacks of intestinal obstruction. On the first two occasions laparotomy was performed and the twisted sigmoid restored to its normal condition. On the other occasions the symptoms of obstruction were relieved by the rectal tube. The operation was performed because the attacks were becoming more frequent. The case will be reported in a future Bulletin with illustrations.

November 5, 1906.

Dr. Barker in the chair.

Exhibition of a Case of Cerebral Palsy. Dr. Amberg.

Child, a male, twenty-two months old, with a history of asphyxiation at birth which lasted some time. The child now shows athetoid movements of the hands when excited, and similar but less marked ones in the feet. Otherwise the hands are held flexed at the wrist and show a certain degree of spasticity. The patelar reflexes are increased and the child, though twenty-two months of age, cannot stand alone and is backward in speech. The athetoid movements, together with the increased reflexes and the history of asphyxiation at birth, make the diagnosis of cerebral palsy definite.

The Topography of the Parathyroids. Dr. MacCallum.

The exact disposition of the parathyroids is of interest, especially to surgeons. The glands are distinct from the thyroid gland developing from a distinct rudiment and their removal in most animals causes tetany followed by death. The tetany may be cured temporarily by bleeding and giving an infusion or by giving parathyroid extract either intra-venously or intraperitoneally. These symptoms are not produced in the goat, pig, sheep, etc., for the reason that the position of the glands not being known they are seldom removed. Partial extirpation in dogs as a rule gives no tetany. If only one gland be left certain strains may bring on tetany as lactation, etc. Tetany in human beings was long thought to be due to removal of the thyroid gland. There are weighty reasons for the surgeons to maintain the integrity of the parathyroids. Dr. MacCallum has prepared a number of charts made from dissections at autopsies, showing the various positions the parathyroids may assume. It is easy to distinguish between the parathyroid and the thyroid. The parathyroid is small and not elastic like the thyroid but soft and mushy. It is not translucent and is of a chestnut or a yellow ochre color, homogeneous. The glands are about eight mm. long or shorter; two mm. wide; flabby and tongue like. The thyroid blood supply is derived from the superior and inferior thyroid arteries and that of the parathyroids from separate and distinct branches of these arteries, which are often quite long. There is a soft, loose areolar tissue covering the thyroid gland and extending back of the trachea. The parathyroids are found in this loose tissue, four in number in more than half of the cases. The number found depends usually on the carefulness of the search. The most frequent, though not constant, position of the glands is—for the upper ones—along the posterior border of the thyroid where the superior artery enters it. The lower gland lies in a notch of the thyroid along its posterior border. This is by no means constant, the upper one may lie near the lower one; this may be symmetrical. Or the upper may be lower still, and the lower one below the border of the thyroid or attached to the lower pole. In some cases one may be found over the trachea. In one case Dr. Whipple found the thyroid on one side completely atrophied, and the superior and inferior parathyroid lay quite independent of it, loose, as it were, in the tissue. The parathyroid is nearly always loosely attached and can be picked up on the stalk of the vessel. In the ligation of the thyroid arteries the ligature must be placed inside of the parathyroid branch which is, of course, more difficult in a tumor of the thyroid. The tetany caused by the romoval of the glands, Dr. MacCallum has found, can be warded off or stopped by injection of the parathyroid extract or feeding the glands by mouth; those of the ox are used, in which animal two are found as brown masses at the top of the thymus on either side.

November 19, 1906.

Benign and Malignant Cystic Tumors of the Female Breast. Dr. Bloodgood.

These cysts vary from the most benign to the most malignant forms of tumors. Not infrequently a differential diagnosis between the benign and malignant neoplasm cannot be made from the clinical history and examination, and the recognition of its exact nature is possible only at the exploratory incision.

A galactocele is due to a dilatation of a duct in the lactating breast. It is a relatively rare tumor. We have observed but one example. The tumor may arise during, or at various intervals after active lactation. The tumor as a rule is somewhat bottle-shaped, with the neck of the bottle towards the nipple. Unless secondarily infected the skin and nipple of the breast remain normal, and the smooth tumor gives the sensation of fluctuation. At the incision there is a distinct cyst wall of connective tissue with a smooth lining; the contents resemble milk. In the majority of cases the remainder of the breast has the appearance of lactation hyper-

trophy, the ducts are usually dilated, and there may be other small galactoceles. Conservative treatment—excision of the cyst only—should be sufficient. I have never observed a malignant tumor to develop in a galactocele.

Cysts in the lactating breast due to chronic pyogenic infection with the formation of a chronic abscess. We have observed one case. In this instance the swelling without any of the signs of inflammation was observed in the upper and outer quadrant, in the fourth month of lactation. When examined four months later, there was a tumor about the size of a fist involving the entire upper and outer quadrant; the nipple and skin were normal, there was no fever; lactation had not been disturbed. The tumor, though smooth and firm, did not have the characteristics on palpation of an encapsulated mass, and did not fluctuate. At the exploratory incision the skin and subcutaneous fat were normal; then the knife passed through breast tissue, the picture of lactation hypertrophy, from which milk exuded; then a narrow zone of condensed breast tissue devoid of milk, then a very narrow zone of the hemorrhagic tissue resembling granulation tissue; the contents were a thin, granular, yellow material, that is, the appearance of pyogenic pus in which the organisms had died and in which the leucocytes had become granular.

Cancer Cysts in the Lactating Breast.—There has been observed one case. It did not differ clinically from the previous case, but at the exploratory incision the wall of the cyst was thicker and more distinct, the lining zone was white and granular instead of red, and the contents were a very thick, granular material, due to broken down epithelial cells.

These three observations demonstrate that during lactation a malignant cyst is possible, and it should be differentiated from the galactocele and the chronic pyogenic abscess.

Simple Cysts.—This term is employed to describe a cyst with a smooth inner surface and a definitely outlined connective-tissue wall of 1 to 3 mm. in thickness; the contents are never hemorrhagic, it is either a clear or cloudy serous fluid. These cysts may occur clinically as single tumors in women from twenty-eight to seventy years of age. Clinically they are always benign. They are most commonly observed at the menopause between the ages of forty and fifty, and the breast usually shows hypertrophy, which I have called senile parenchymatous hypertrophy (Surgery, Gynecology and Obstetrics, December, 1906, vol. iii, p. 721).

When these tumors are multiple in one or both breasts (a very common occurrence) a clinical diagnosis is not difficult, but when they occur as a single tumor they cannot always be differentiated clinically from the cancer cyst, or the solid carcinoma. Their recognition, at the exploratory incision is not difficult. For details I refer to the above reference.

Cysts with Intracystic Papillomata.—In the majority of these cases there is a history of discharge of blood from the nipple, and quite frequently at the examination blood can be expressed. This history or finding may be considered pathognomonic. At the exploratory incision the character of the cyst wall differs very little from the simple cyst; it may be thicker. But within the cyst one can see or feel a papillomatous growth. The presence of blood in such a cyst is not a sign of malignancy. In the experience, however, of this clinic, we have had an equal number of benign and malignant intracystic papillomata. When the evidence of malignancy has not been indicated clinically by retraction of the nipple, adhesions of the skin, or infiltration of the breast around the tumor, one can demonstrate malignancy, if present, by studying the base of the papilloma. In the benign tumor the distinct cyst wall is present beneath the papilloma; in the malignant tumor this wall and the breast tissue beyond are infiltrated and have the appearance of carcinoma.

The Cancer Cyst in the Non-lactating Breast.—The true cancer cyst has a distinct cyst wall which may resemble somewhat the wall of a simple cyst or one containing a papilloma. As a rule, however, the wall is thicker, and if carefully studied the naked-eye appearance of carcinoma should be present. The diagnosis, however, can be readily made from the contents of the cyst. In the majority of cases this is hemorrhagic. So far in the experience of this clinic, a cyst containing blood without an intracystic papilloma to explain the hemorrhage, has always been a malignant tumor. When blood is absent the contents are very thick and granular, differing characteristically from the contents of a simple cyst or a galactocele.

One should look out for these tumors, because they frequently present themselves with all the clinical features of a benign growth, and if a surgeon excises them without careful investigation he will be surprised to learn when the wall is studied histologically, that he has treated a malignant tumor of the breast conservatively, and the probabilities are that a secondary complete operation will not accomplish a cure.

Sarcoma Cysts.—Solid sarcoma of the breast is a relatively rare tumor, and until recently I had never observed a cyst of the breast due to the degeneration of a sarcoma. Such a specimen was sent to the laboratory by Dr. Pancoast. Clinically it was apparently a benign tumor in a woman over sixty. The contents were chiefly clear fluid, but the wall of the cyst was entirely different from a benign cyst; it was composed of soft, friable, granular tissue, here and there with specks of blood. It proved to be a perithelial angiosarcoma. I have observed a similar case in the scalp, which was diagnosed a wen, and one between the skin and mucous membrane of the cheek, looked upon as a blood cyst. In these two cases the contents were hemorrhagic.

Dermoid Cysts.—I have observed five benign and one malignant tumor of this character so situated subcutaneously in the breast that they had all the appearance of a primary breast tumor. In the benign dermoids the wall was thin, easily enucleated, and the contents typical of a dermoid. In the malignant tumor the wall was thick (3 by 5 mm.), not easily separated from the surrounding tissue, and on section it had the appearance of carcinoma. The contents, however, did not differ from that in the benign tumor.

(A number of pictures were shown on the screen illustrating the various types of cysts of the breast.)

Typhoid Spine. Dr. MacRae.

The term typhoid spine was introduced by Dr. Gibney, of New York, in 1889, to designate a certain group of cases, the chief points concerning which are as follows: The condition generally comes on in convalescence and not later than three months after the attack. Pain is the most marked feature. There is a distinct tendency to recover. Certain sensory symptoms are present. Gibney considered it an inflammation of the soft parts holding the vertebræ together. Concerning the actual condition, however, there was a difference of opinion, chiefly between two factions.

Gibney declared it to be a definite organic condition, while on the other hand there were those who believed it to be entirely a functional disorder without any organic change. The first view was somewhat at a disadvantage, since the condition was never fatal, there were no autopsy findings to confirm their belief, while in favor of the second view there were several points. First the condition was only one of symptoms; secondly, the patients always got well; suppuration never occurred. This last was one of the strongest arguments against it being an organic change caused by the typhoid organisms, for, as is generally known, typhoid lesions nearly always suppurate.

Later, however, more men becoming interested in the subject, interesting reports of certain changes were made, such as kyphosis, lateral curvature, and signs of local inflammation (there was in no case, however, any report of suppuration); changes in the lower extremities, such as wasting, changes in the reflexes and sensation, all of which are suggestive of organic changes.

It has only been recently, however, that the organic change has been really recognized. Two cases that we have had here had important changes worthy of note. The first case had had typhoid fever about three months before. The condition began with a sudden pain in the back and in a short time he could hardly move; on his admission he could scarcely be touched, so that only an unsatisfactory examination could be made. Physically nothing was found, but the X-ray showed deposits of bone along the spine in the lumbar region. A few days after admission the patient had a relapse; he improved gradually and three months later when discharged he had a little limitation of the spine and the X-ray showed an increase in the bony deposit.

The second case showed very much the same condition on admission as did the other patient. On discharge two of the intervertebral discs and the lateral ligaments showed bony changes. The infection was with a paracolon organism.

Clinically we have nowhere a condition the equal of the neurotic condition seen in typhoid spine. We have a patient progressing favorably; within three or four days he shows a complete transformation to a whining, complaining creature, crying for no particular reason except that he cannot help it. The pain is helped very little by sedatives, morphia is only helpful in large doses, say a half grain, which probably will have to be repeated.

Certain local changes may be seen, such as redness and swelling. In the legs we have changes in the reflexes and sensation, with probable wasting, which speak, however, for an organic change in the spine. There is without doubt in some cases a bony deposit but we cannot say that in all cases we have an organic change.

Turning to spondylitis deformans we find a clinical picture similar to the typhoid spine, the same marked neurotic condition, the same tendency to get well but often with more severe symptoms; in fact a fairly exact parallel can be drawn between the two. In the arthritis deformans all conditions exist from that in which the whole spine is involved to that in which there is very little pain, so in typhoid we may have the different conditions from the severe to the mild.

Since arthritis is rare in typhoid it does not seem that all are arthritis, and since suppuration is so common in periostitis we cannot go further than Gibney, whose description was a change in the ligaments, periostium, and perhaps in the intervertebral discs.

From the findings of the spinal changes and the clinical conditions, as far as we can tell, we have here two parallel conditions. Since we believe the etiology of arthritis deformans to be infectious we have here two organisms that can cause like changes, namely, typhoid and the paracolon bacilli. The influenza bacillus may be the cause also in some instances. Therefore we may believe arthritis deformans to be due to many different organisms.

There is one point, though, that is not clear—why is it that suppuration does not occur in typhoid spine? It is always dangerous to prophecy, but if this view is correct it is most probable that suppuration will be reported.

To review briefly:

1. Bone changes have been demonstrated in typhoid spondylitis.

2. A comparison of typhoid spine with spondylitis deformans shows conditions partially parallel.

3. Evidence favoring the view that arthritis deformans is due to some infectious agent.

In conclusion it is suggested that the name typhoid spondylitis be substituted for the old name of typhoid spine in spite of the fact that it is so firmly fixed.

A Case of Congenital Cystic Kidney. Dr. Gorter.

Clinical features.—On October 23, 1905, Dr. Cole showed the patient before the Medical Society and gave his history, which in brief is as follows: A man, age 41, with a complaint of shortness of breath and a weakness in the lumbar region; the date of the onset is not known; he had had albumen in his urine for eight years. Two years ago his color changed, he became cyanotic, also pigmented over the cheek; there were signs of cardiac weakness.

The abdomen became enlarged but there was no discomfort,

there was more or less ascites; as the ascites decreased a mass could be felt in the left flank. There was also on the right side a tumor-like mass extending downward into the pelvis; this mass could be lifted forward. There were definite symptoms of cystic kidney polyuria, low specific gravity, and as a late symptom, bloody urine, also albumen and casts in the urine. The hæmaturia, Dr. Cole thought, to be due to a rupture of small vessels in the cyst walls. Over the forehead and cheek there was pigment. Diagnosis cardiac weakness, hæmaturia, chronic nephritis, and tumor.

In June, 1906, he first came under the observation of Dr. Gorter. The complaint then was indigestion and general lassitude. The abdominal examination was the same as above, the urine was alkaline and contained hyaline casts. On July 12, 1906, his temperature was 103° and the pulse rapid and weak; there was dyspnœa and precordial pain. A pericardial friction rub developed which gradually decreased as the cardiac dullness increased. The temperature varied between 100° and 103°. Uræmia developed later with delirium and coma, and death followed from œdema of the lungs.

Autopsy Report. Dr. Whipple.

Anatomical diagnosis.—Congenital cystic kidney, extreme arterial sclerosis, organizing pericarditis, broncho pneumonia, congestion and œdema of the dependent parts of the lung, cardiac hypertrophy and dilitation with diffuse fibrous myocarditis, general pigmentation of the skin, marked flattening of the adrenals.

The kidneys filled both flanks completely, forcing the intestines into a small gutter, as it were, between them; together they weighed 5200 grams. They were made up of bunches of cysts of all sizes; many contained fluid, some colloid material, others old blood clots. The pelves were fan-shaped; the ureters normal. The adrenals were flattened between the upper poles of the kidney and the diaphragm. Dr. Cole's theory of the pigmentation was, that it was due to compression of the adrenals, but the microscopic examination showed nothing to account for it, there was fatty degeneration of the cortex, the medulla was normal. It was possible that the pigmentation was due to the same cause as exists in abdominal aneurysm or any large abdominal tumor. The liver weighing 2900 grams, was also cystic, the cysts as a rule having smooth lining, some contained fluid, some a colloid material.

In the kidneys many of the glomerulæ had thickened capsules, there was also a thickening of the tissue between the tubules, many of which contained blood casts and fresh blood.

In the pancreas there were many cysts formed from the duct and lined by cuboidal epithelium.

Section of the liver, kidney, and pancreas were shown under the microscope.

Dr. Whipple also reported another case of congenital cystic kidney in a female child from the Obstetrical Ward who lived but 45 days. The anatomical diagnosis—double cleft palate, anæmia and emaciation, double uterus, double ureters and pelves of kidney, the ovaries and tubes normal. To the naked eye the kidneys were normal but under the microscope they were seen to be full of small cysts from dilated tubules; some of the glomerular capsules were dilated more or less, and some of the capsules had ruptured into neighboring ones; some of the glomerulæ were of a rudimentary type as in congenital syphilis. This is a point in favor of the idea that the cysts are due to a congenital defect rather than a cystic development. The tubules showed casts, the stroma was slightly increased.

December 3, 1906.

Meeting of the Johns Hopkins Hospital Medical Society. Dr. Barker in the chair.

Exhibition of Cases. Dr. Harvey Cushing.

Case I. *Decompressive craniectomy for brain tumor.*—This patient is 61 years of age. He entered the hospital November 12, complaining of headache, of loss of vision, and difficulty of speech. He has enjoyed fairly uniform good health until the past summer, when he began to suffer from headaches. They have been occasionally frontal, occasionally occipital; have been most profound at night and have for some months given him much discomfort, although they have not completely incapacitated him.

On October 9 a sudden accession of symptoms followed some unusual exertion. His headache became worse; there was considerable vertigo, pallor, and nausea. There was no loss of consciousness. When these acute symptoms had subsided it was found that the patient was markedly aphasic. His understanding of spoken language was somewhat affected, though he vocalized normally; he misused words and his speech was greatly confused; his ability to read written language was affected as was also his ability to write or copy.

His headaches persisted and a few weeks later it was found that he had a double choked disc with hæmorrhages. At about this same time some weakness in the right external rectus muscle became apparent and there was considerable diplopia. His vision, too, began to fail, so that objects were dim, and his visual acuity was much reduced. These perimetric charts taken by Dr. Bordley on November 12 show not only that the field of vision had become constricted but that there was a right, lower quadrantal hemianopsia.

On November 13 a decompressive operation was performed according to the subtemporal method which I have described. The bone underlying the temporal muscle was removed and the dura freely incised to the edges of the bone defect. The brain was found to be under considerable tension. You will see that the wound has healed perfectly, leaving an almost imperceptible linear scar, and that the protrusion is so slight that it would hardly be noticed unless attention were called to it.

The operation has accomplished, not only what it was hoped it would accomplish in relieving the patient's subjective discomforts, but it has done more than that. The palsy of the abducens has completely cleared up, showing that it was probably a pressure palsy alone, for the sixth nerve suffers more often and more quickly than any other of the cranial nerves as a result of various conditions of intracranial tension. The choked disc has entirely subsided. These charts taken yesterday, three weeks after the operation, show that the visual fields have increased almost to their normal limits, leaving, however, as before, the quadrantal notch where there is complete absence of vision, evidently due to the destructive lesion. The patient's aphasia, too, has rapidly cleared up. His speech is much improved and he uses words with only an occasional error. He writes plainly

and understandingly, both spontaneously and to dictation, as this specimen of his handwriting will show. He is able to read understandingly even the small print of the daily newspaper.

His headache, gastric disturbances, vertigo, etc., have entirely disappeared. He sleeps soundly, as he has not done for months; eats with appetite, and is rapidly gaining weight and strength.

We have now had about thirty cases of decompression by this method, the majority of them having given immediate relief, and in many cases with as striking a result as is shown in this patient. I have come to believe that every patient should be operated upon in some such way as this as soon as the diagnosis of intracranial tumor has been made. Operation is especially urgent, as others have said, in case a choked disc has appeared, but I do not think that we should even wait for the appearance of a choked disc. Even if the trouble is possibly of a luetic nature I think the operation should be done first and the drug treatment carried out secondarily, because it is often difficult to distinguish between luetic and actual neoplasms, and it can do the luetic no harm and may save time and loss of ground in case the trouble should prove not to be of luetic origin.

In regard to the desirable place for decompression, I am aware that my views disagree with the opinion that has been expressed by some others, namely, that it is wise to decompress over the suspected situation of the tumor. In this patient, for example, we suspect that the trouble is situated somewhere in the postcentral part of the left hemisphere, possibly near the occipital lobe. If the decompression had been carried out in that situation we would have had a large and obtrusive hernia. As it is, the temporal muscle prevents the undue formation of a hernia and yet allows a sufficient protrusion to relieve symptoms. On two occasions I have seen disastrous results from carrying out a decompression according to this advice, namely, to decompress over the tumor. These were cases in which it was thought possible that the tumor might be found and removed. In both cases the tumor was a vascular glio-sarcoma, situated beneath the cortex, and in both cases the removal of the overlying bone and dura, with the relief of tension and the consequent bulging of the brain, led to the rupture of the poorly developed vessels of the tumor and to a great increase in size of the tumor on account of the hæmorrhages which had taken place. For this reason it may perhaps be unwise in certain cases, to decompress, directly over the growth.

Contrary to the opinion held by many, that only those cases of cerebral tumor should be operated upon in which there are localizing symptoms, I feel that the cases which are *most favorable* for operation are those in which there are no localizing symptoms whatsoever. For in these cases it is possible to relieve the underlying symptoms, and inasmuch as the tumor is implicating some silent area of the brain, it may, in case it is a slow growing tumor, continue to enlarge for months or perhaps years without damaging in any way the more important centers. On the other hand, if the growth has already so damaged centers as to enable us by our as yet gross methods of diagnosis to determine its situation, it has incapacitated the patient to such an extent that decompression merely for the relief of subjective symptoms is much less satisfactory than it would be under these other circumstances. Furthermore, operation and removal in such cases of cerebral tumor as indicate their presence by irritative or paralytic symptoms means, usually, a persistence, if not an increase, of these same symptoms.

Case II. *Gasserion ganglion operation for major neuralgia.*—This old man, 79 years of age, represents my forty-eighth case of ganglion extirpation. Although in years not the oldest patient—for one of the recent operations was conducted on an old gentleman of 89—nevertheless, he represents the type of neuralgic who is old in his physical condition; so old in fact that one hesitates to subject such a patient to a supposedly critical operation.

He has suffered from neuralgia for twelve years, and during that period has undergone six of the so-called minor or peripheral operations, the traces of which you will see by these supra- and infra-orbital scars, which have so drawn upon the eyelids as to lead to a certain amount of ectropion. During the past twelve years these operations have succeeded in giving him about five years of relief; in other words, they have afforded periods of relief averaging only six months. He has, of course, after each operation been apprehensive of the return of pain, which of late had become very severe and which finally involved the entire trigeminal territory. He, furthermore, had been so thoroughly drugged that sedatives and narcotics in large doses were a daily necessity. He is markedly arterio-sclerotic and has a bad heart with a mitral lesion.

His operation, performed two weeks ago, has left what I have heretofore spoken of as an "invisible scar," and I doubt if any one unaware of the nature of the operation, could have found evidence of this procedure other than by the slight pulsation which you doubtless may be able to see in the temporal region.

In this case I have made use of the more recent methods of conducting this difficult operation, for our methods improve as experience is gained. You will see that he is able to raise his eyebrows symmetrically; in other words, the upper division of the facial nerve has been preserved. You will see that there is no flattening whatsoever—nor will there be subsequently—of the face in consequence of the paralysis of the masticatory muscles, because of the careful preservation and closure of temporal muscle, fascia, galea aponeurotica, and other layers of tissue in the temporal region. Furthermore, in my last twenty cases I have not removed the ganglion itself, although the ganglionic part of the operation has been conducted in a way closely similar to that detailed in my original paper describing the approach under the meningeal artery. However, instead of freeing, as used to be done, the first, second, and third divisions, and lifting the ganglion from its bed—the more bloody part of the operation—the liberation is conducted only between the meningeal artery and the third division. Thus, after this posterior portion of the glangion is well freed from the surrounding envelope by means of a specially made dissector introduced behind and under the ganglion, the sensory root is evulsed from the pons just as is done in the operation of total extirpation, and the root is thus tilted forward over the ganglion so that a gap of about 2 cm. is left between ganglionic structure and pons. Were it not for the troublesome bleeding which comes from liberation of the first and second divisions it would be very easy to remove the ganglion. It, however, is left in its position and this saves considerable time in the conduct of the operation.

One can never tell, however, how long a time one of these operations will require. The procedure in this particular case required two hours. In another patient operated upon a few days before

him, only thirty minutes were needed—the shortest period in which I have ever carried out the procedure. In still another patient, operated upon only two days ago, three hours were required, inasmuch as I found a most unusual condition, namely, a ganglion covered by a shell of bone so that it was necessary to chisel through bone before the ganglion could be exposed. This, however, is such a rare anomaly that it need hardly be taken into consideration.

I know of no group of surgical patients in whom operative measures give more satisfaction than these particular cases. It, however, is difficult and specialized work, and it is only due to the observation of the veriest detail, to the constant study of anatomical conditions and to unusual familiarity with the operation that it may be carried through with comparative safety. In my last twenty-five cases there have been no deaths and no complications, and out of the forty-nine cases I have lost only two. Had I been as familiar with the procedure at the time these two fatal cases were operated upon as I am now, I am sure that these two patients would have been saved. The mortality is generally spoken of as ranging in the neighborhood of twenty per cent, and I doubt very much if this mortality will be lowered except in the hands of those who devote themselves particularly to this form of work.

There are many interesting physiological conditions upon which light has been thrown by the study of these recent cases. Dr. Bordley and I have found in all of them a transient choked disc, which further strengthens our view that choked disc is a matter of mechanical rather than toxic origin. We have found that only in those cases (unusual in our recent series) in which there is a temporary pressure palsy of the abducens is there a narrowing of pupil and palpebral nerve evidencing sympathetic palsy. Removal of the ganglion alone and its three divisions does not necessarily lead to narrowing of the pupil, and hence we are led to believe that the sympathetic fibers run with the sixth nerve. There are many other points in regard to physiology of the trigeminus—its motor distribution, its area of anæsthesia, its relation to taste, etc.,—which I would be glad to speak of here but must defer to a subsequent occasion.

There is one physical peculiarity of many of these patients which may be mentioned, namely, their arterio-sclerosis. Sclerotic changes in the vessels of the ganglion have been found and described by some pathologists as the possible cause of the neuralgia. I am inclined to believe that arterio-sclerosis is a result rather than a cause of the pain. Before his operation this old gentleman had a systolic pressure of about 190 which would rise to 250 or over during his paroxysms. I think it possible that these constantly recurring afferent impulses, like hard work or alcohol in excess, may finally lead to changes in the vessels, from their being subjected to the oft repeated unnatural strain over a period of years. Since his freedom from pain, the blood pressure in this old man has averaged about 140.

The main reason for bringing this patient before you is to show how absolutely inconspicuous is the operation when done by our present day methods. Needless to say, it is the only way of permanently relieving these unfortunates from pain and of restoring them to a life of uninterrupted activity.

Case III. *Exploratory craniotomy for Jacksonian epilepsy, originating in the motor area of the lower extremity.*—This patient was shown to the Society three weeks ago by Dr. H. M. Thomas, who went fully into his interesting history. He has had, as you will remember, Jacksonian fits for the past ten years, these fits beginning with a sensory aura followed by motor twitching in the left leg. For the past six years the attacks have become frequent and many of them are associated with unconsciousness.

Early in 1903 he suffered for some months with headaches and at that time his vision began to fail. He has been under Dr. Thomas' observation for the past year and a half, and an exploratory operation has been postponed, owing to the fact that Dr. Thomas regarded many of his more serious symptoms as quiescent. The examination of the eyes has shown a narrow visual field with a stationary degree of double optic atrophy, and the conditions make it seem probable that this atrophy has been consequent upon a choked disc. It would seem likely that the patient has a tumor involving the superior limit of the paracentral convolutions but which has ceased to give pressure symptoms and only leads to these Jacksonian attacks through some form of irritation. Knowing that in this particular field the upper portion of the motor strip underlies the lateral expansions of the longitudinal sinus, Dr. Thomas did not feel that he could advise an operation very strongly, nor did I undertake it without some misgivings.

On November 22, under ether anæsthesia, a large bone flap was turned down in such a way as to expose the upper areas of the primary, motor, and sensory fields, and the adjoining part of the right hemisphere. The patient took his anæsthesia badly and, although I do not believe in the wisdom of a two-stage operation as a routine for brain tumors, it seemed, in this case, unwise to proceed; the opening of the dura consequently was left for a second stage. The bone flap was replaced; the wound in the scalp was closed. I had some hesitation in tightly closing the wound, inasmuch as there was some oozing from the dura corresponding with the exposed lateral expansion of the sinus, namely, where Pacchionian granulations projected into the sinus and where there were communications between the sinus and the overlying diploe, which communications had been torn when the bone flap was elevated. It was hoped, nevertheless, that the pressure of the flap would be sufficient to stop this slight oozing.

Realizing, however, that the oozing might continue, a blood-pressure apparatus was in continual use during the rest of the day and night, and the patient's pulse was recorded frequently. I saw him four hours after the operation. He was then conscious, comfortable, feeling in no way upset by the procedure.

He passed a very comfortable night and not until the early morning hours was there evidence that anything was going wrong. At 5 a. m. his pulse, which had been about normal, dropped to the 60's, and two hours later it registered as low as 54. He had become somewhat drowsy.

When I saw him at 9 o'clock in the morning it was a little difficult to arouse him, though when aroused he said that he felt comfortable and felt no pain. His pulse was slow, his blood-pressure had begun to rise, and there were, even on palpation, distinct rhythmic waves in the tension of the pulse, waves not only in its tension but in its rate, and these waves were likewise accompanied by perceptible alterations in the depth of his respiration. At the same time an ophthalmoscopic examination showed a high grade of choked disc; even on top of his atrophic nerves the œdema was so great that it measured 4 diopters. It is to be remembered that before the operation there

was no œdema whatsoever of the retinæ. Dr. Eyster, whose observations have done so much to throw light on the physiology of Cheyne-Stokes respiration, made at this time some careful charts, which I hope he will demonstrate to you, for they show definitely the rhythmicity of pulse-rate, blood-pressure, and respiration.

It was quite evident that the patient was approaching Kocher's *Höhestadium des Hirndruckes*, and preparations were made to reopen the wound. This procedure, however, was unavoidably delayed, and not until 12 o'clock of that day, eight hours after the first onset of symptoms, were we able to determine, on opening the wound, what it was that had caused the pressure symptoms. The dressing was removed, the sutures holding the anterior edge of the incision were divided, and no sooner was this done than the bone flap dislocated itself outward and a large, black, extradural clot, fully 3 cm. in thickness, began to ooze from the wound. The patient, who by this time had become so profoundly unconscious that he failed to respond to stimuli, immediately turned his head over, opened his eyes, and said, "Why, good morning." Though all of this proved very spectacular, the real reason for recording this case is to show the importance of careful observation, on physiological grounds, of patients in whom there is any postoperative likelihood of complications from intracranial hæmorrhage. The clot was scraped away and the partially reopened wound filled with iodoform gauze, and the patient returned to his bed. He had no further symptoms of compression and the œdema of his eye grounds rapidly subsided.

On November 27, five days ago, the second stage of his operation was performed; the dura was opened, and although the usual difficulty was experienced in exposing the leg centers, we finally succeeded in getting a clean, dry exposure, and no cortical evidence whatsoever of a tumor was found. The exposed cortex was faradized and in this patient for the first time I succeeded in eliciting clean-cut movements from thigh, lower leg, and foot. It is unusual to have this inaccessible edge of the hemisphere so freely exposed as to allow of cortical stimulation. The dura was then closed, the bone flap replaced, and the scalp once more resutured. You will see that, despite this second closure and the six days of partial opening of the wound, the healing has been almost as perfect as it is in the general run of these cases which have been permanently closed at the first sitting.

The case is chiefly interesting from its physiological side, demonstrating as it does the early phenomena of compression, their timely recognition, and their immediate subsidence after removing the source of pressure. From a therapeutic point of view we have accomplished nothing. However, it may be said that in case one can accomplish nothing, the next most desirable thing is to do no harm, and I am glad to say that in this poor fellow's case we have gotten out of our operative difficulty without damaging him. As is usual in these exploratory operations for epilepsy, even when nothing is found, he expresses some subjective sense of betterment and as yet has had no return of the mild type of his epileptiform seizures. I do not, however, anticipate that this apparent benefit will be of any considerable duration and there is no reason to believe that his attacks will not continue as before.

If our focal diagnosis has been correct, either the growth is a subcortical one, or else it lies on the mesial surface. A all events it is certainly inactive at present and for three years has not led to any increase of tension sufficient to give pressure symptoms; nor did we find any evidence of increased tension at the time of operation.

Cases of Thrombosis of the Posterior Cerebral Artery. Dr. Thomas.

Two years ago Dr. Thomas showed a patient with thrombosis of the posterior cerebellar artery, and last summer a patient died in the hospital of the same trouble. The picture presented is one of a remarkable combination of symptoms; Dr. Thomas has collected twenty-five cases corresponding to this picture. Among these there have been seven autopsies reported, besides those of Dr. Thomas. A microscopic examination shows a softening in the mid-olivary region, and a thrombosis of the posterior inferior cerebellar artery has either been found, or assumed. Dr. Thomas called attention to Mr. Burrows' work done in Dr. Mall's laboratory, on the anatomical distribution of this artery. The disease occurs usually in men somewhat above middle age, with a sudden attack of vertigo, and rarely loss of consciousness. There is a tendency to fall in one direction and a pain on the same side of the face towards which they tend to fall; and a difficulty in speech and swallowing, accompanied at times with persistent singultus. The initial symptoms last for a shorter or longer period, some of the patients being in bed for a year on account of the vertigo. On examination an interesting picture is found: if the patient sits up or stands he tends to fall to one side always. The visable perspiration is on the side opposite to that towards which he falls; he is apt to have a difficulty of speech from paralysis of the vocal cord on the side toward which he falls; there is also a certain amount of ataxia in the limbs on this side and a slight ptosis with contraction of the pupil.

Sensory examination shows on the affected side a loss of pain and temperature on the face and the same loss on the contra-lateral arm, body, and leg.

The history of the man who came into the hospital this summer and died is as follows: He was somewhat of a nervous or hysterical temperament. Six weeks before admission he had an attack of vomiting, three weeks later he had an unconscious attack, was unable to swallow or speak and the pupil was smaller on one side with a ptosis on that side also. On examination there was found a marked arterial sclerosis and the patient was somewhat out of his head. There was thrombosis of the vessels of one leg, the lungs, heart, and kidneys were involved; temperature was 100°. Sweating was apparent only on one side, on the opposite side ptosis and a small pupil, and a loss of pain and temperature in the distribution of the V, was present. At autopsy there was found a thrombosis nearly everywhere, but no thrombosis was evident in the posterior cerebellar artery as was expected. However, on microscopic examination, this artery was found completely thrombosed, and a softening of the lateral aspect of the medulla in the region just outside of the olive.

Among the interesting points to be explained is the crossed dissociated sensory distribution. This is believed to be due

to involvement of the descending root of the V, and Gower's bundle, conducting pain and temperature from the opposite side of the body. The ataxia, and the falling to one side, are due to involvement of tracts which reach the cerebellum by the restiform body. The slight ptosis, the small pupil, and the lack of sweating are due to the involvement of the sympathetic tract in the medulla. Just where the tract is, is not known.

Some Observations on the Action of Lipase. Dr. Loevenhart, G. Peirce, and C. G. Souder.

Six years ago Dr. Kastle and Dr. Loevenhart demonstrated that lipase is reversible in its action on ethylbutyrate; that is, it is capable of forming the ester from ethyl alcohol and butyric acid, as well as effecting its decomposition into these substances. Lipase accelerates the reaction in either direction. Later Dr. Loevenhart demonstrated lipase in greater or less activity in most of the tissues tested. This work suggested a simple explanation of the fat absorption from the intestine, its translocation and deposition in the tissues and its utilization during inanition. Later lipase was shown by Hanriot to be reversible in its action on monobutyrin and others have demonstrated synthesis of triolein by the action of lipase. Up to the present work no extended study has been made to determine whether the hydrolysis of different esters by different tissues is always due to some enzyme. During this work of Loevenhart, Souder, and Peirce two interesting problems arose, namely: (1) The effect of bile upon the hydrolysis of esters by pancreatic juice; (2) the action of sodium fluoride on the hydrolysis of the various esters. The general view of the function of the bile in the absorption of fat from the intestine has been that it dissolves the fatty acids formed and emulsifies the fats and that its action is therefore simply physical. The solvent and emulsifying action has been attributed to the bile salts. Hewlett, last year in the J. H. H. Bulletin, made the observation that bile accelerates the hydrolysis of the water-soluble ester, triacetin by pancreatic juice, twenty-six times, while pancreatic juice alone has comparatively little action on it. The action of the bile in this case could not be attributed to its emulsifying and solvent action. Hewlett believed the acceleration to be due to the lecithin contained in the bile.

Loevenhart, Souder, and Peirce have studied the effect of bile salts, lecithin and bile on the hydrolysis of a series of esters by pancreatic juice. Their results are in brief: (1) These mixtures all accelerate greatly the action of pancreatic juice on all of the esters studied. (2) The effects of these substances, especially the bile salts, vary enormously with the concentrations employed. Thus the amount required to accelerate the action on triacetin has practically no effect on the hydrolysis of olive oil and the quantity required to accelerate the action on olive oil greatly inhibits the action on triacetin. (3) The accelerating effect on the hydrolysis of one ester is no index of its effect on another ester. (4) The accelerations noted with lecithin and bile salts vary with different specimens of juice; in some cases the former, in others the latter causes the greater acceleration. They believe that it is chiefly the bile salts that cause the accelerating action of the bile, under physiological conditions, and agree with Hewlett that their action is not altogether due to their solvent and emulsifying action.

They offer no explanation of the mechanism of the acceleration noted in the hydrolysis of esters when the pancreatic juice is mixed with bile salts, lecithin, or bile.

As to the action of sodium fluoride on the hydrolysis of the various esters, Kastle and Loevenhart found sodium fluoride, 1-5000, greatly inhibits the hydrolysis of ethyl acetate and ethyl butyrate by the liver and pancreas extracts. The idea in this work was to determine whether it retards the hydrolysis of the higher fats as well as that of the lower esters. All of these processes are retarded by the fluoride, but the concentration of fluoride required varied enormously with different esters. The acid from which the ester is derived determines the inhibiting effect of the fluoride.

The inhibiting action of the fluoride decreases with increasing molecular weight of the acid from which the ester is derived. Thus hydrolysis of the esters of acetic acid is about 15 times as sensitive to the fluoride as that of ethyl butyrate, and the hydrolysis of ethyl butyrate 100 to 1000 times as sensitive as that of olive oil.

The hydrolysis of the lower esters is remarkably sensitive to the fluoride. Even in concentrations of 1 to 100,000,000 some inhibition is noted. When dilutions beyond the limits of inhibition were used acceleration was frequently noted. Similar facts have been observed in many other enzyme processes.

It was found that the ratio between the activity of the liver and the pancreatic extracts, when tried on different esters, was far from constant. In fact it decreased in an orderly way with the increasing molecular weight of the acid from which the ester is derived. With ethyl acetate the liver was found, in one case, to be about eleven times as active as the pancreas, while with olive oil it was about one-seventh as active as the pancreas. This indicates that the ester-splitting enzymes of the liver and pancreas are different. However, the liver does not contain a specific inhibitor nor the pancreas a specific accelerator for the hydrolysis of the higher fats, as was at first suggested. This was proved by studying the action of a mixture of liver and pancreatic extracts on ethyl butyrate and olive oil.

It was also found that the pancreas of different individuals of the same species varies in its relative activity towards two esters, and much larger variations are noted when different species were studied. These variations are believed to be due to variations in the substances mixed with the enzyme. The same is true of the livers of different species.

It must be borne in mind in considering the identity of different enzymes that, in all the enzymic preparations hitherto obtained we have, in addition to the catylitic substance or mixture of substances, *i. e.*, the enzyme, an unknown quantity

and number of admixtures, the effect of which must, for the present, remain unknown. This admixture is often of the greatest importance. Thus the work of Magnus and the writers has shown that, in addition to the enzyme, the bile salts are essential in the hydrolysis of amyl salicylate by liver extract. The physiologist may look upon the bile salts as an essential part of the enzyme which hydrolizes amyl salicylate.

Some acid is also essential in the hydrolysis of proteids by pepsin. It is suggested that the bile salts and the acid, which can readily be separated from the enzymic preparations should be called coferments. All of the hydrolytic enzymes at present known are destroyed by heat, are non-dialysable, and are catalytic in their action, as far as this has been studied. It is to such a mixture of substances that the term enzyme should be restricted at present, and the term coferment can designate those substances which fail to have any of the above properties, but which are essential to the action of the above group.

Discussion.

Dr. Barker.—I think it is fortunate for us that studies of this kind are being carried on at this medical school. We used to think that the methods of bacteriology were delicate, but evidently they are gross and crude contrasted with the fineness of some of the modern chemical methods. I am interested in hearing Dr. Loevenhart say that he regards the lipase of the liver as distinct from that of the pancreas. The recent work of Magnus indicates that the lipase of the intestinal juice and that of the gastric juice are also different from pancreatic lipase, inasmuch as the latter has its activity greatly increased by glycocholate and taurocholate of soda (synthetic), while the former do not.

I should like to ask Dr. Loevenhart if he has tested the relation of the action of sodium fluoride in connection with the splitting of bodies stereochemically allied to lipase. From some recent work done by Otto Warburg it would seem that lipase itself is less sensitive to stereochemical influence than is the protolytic pancreatin, for while pancreatin acting upon inactive leucinester splits only one of the components, giving rise to l-leucin, leaving the d-leucin-ester unsplit, whereas lipase splits some of both esters, it would be interesting to know whether the effect of sodium fluoride on the action of lipase is more sensitive to stereochemical influence than the lipase itself.

NOTES ON NEW BOOKS.

Tumors, Innocent and Malignant. By J. Bland-Sutton, F. R. C. S. Fourth edition. (*Chicago: W. T. Keener & Co.*)

The demand for a fourth edition speaks well for the popularity of this well-known volume.

The present edition contains over a hundred more pages than the previous one, and numerous new illustrations. There is also a different arrangement of chapters and the main groups of tumors have been somewhat revised and added to, the author arranging them as follows: Group (1) connective-tissue tumors, (2) tumor diseases of the teeth—odontomata and dental cysts, (3) epithelial tumors, (4) tumors arising from the chorionic villi, (5) teratomata and dermoids, (6) cysts.

The chapter on gliomata seems rather brief considering the interest recently shown in regard to this group of tumors. The chapter on sarcomata of bone is even more fully considered than it was in the excellent chapter in the previous edition. The section dealing with neuromata and allied conditions of the nervous system is of particular interest.

Numerous passages on the homology of tumors and other examples of vicious development in lower animals are interesting and suggestive.

The section on carcinoma of the breast, though given more space than in the previous edition, is still not as complete as the importance of the subject demands.

The illustrations are numerous and good, those showing the gross appearance being superior in general to those of the microscopic structure.

The lists of references at the end of the chapters is more extensive than in the previous editions and the index is well arranged.

American Practice of Surgery, a Complete System of the Science and Art of Surgery, by Representative Surgeons of the United States and Canada. In eight volumes. Edited by Joseph D. Bryant, M. D., and Albert H. Buck, M. D., of New York City. Volume I. (*New York: William Wood & Co., 1906.*)

According to the preface this work is intended to portray surgery as practiced to-day in the United States and Canada, and to this end, at the risk of much repetition, numerous surgeons of note, scattered over a wide territory, have been asked to contribute to it.

The first volume of this System of Surgery, which bids fair to be a very extensive and voluminous one, is a large, unwieldy tome of 797 pages. Among the contributors to it are Warthin of Ann Arbor, who writes on "Inflammation"; Galord of Buffalo, who writes a chapter on the "Parasitical Relations of Cancer"; Bloodgood of Baltimore, who contributes an article on "Surgical Shock"; Bryant of New York, who writes on "General Surgical Diagnosis"; Dodd and Osgood of Boston, who describe the "Technique of Radiographic Work"; and several others.

The introductory chapter by Stephen Smith on "The Evolution of American Surgery" is quite interesting. The contribution of Dodd and Osgood, which is illustrated by numerous beautiful radiograms is very instructive and well worth reading.

I can hardly see the place which such a surgery will fill. It is too extensive for the ordinary student body and, being almost devoid of references to the literature, will not appeal to more advanced students. W.

Volume II of the above system compares favorably in general interest with the first; Gibney, Pilcher, Tilton, Willard, and others have contributed articles. It is, like the first, divided into five parts, including tuberculosis and syphilis, surgical diseases of various structures of the body, simple and complicated wounds, diseases caused by heat, cold, and the electric current, and a chapter on skin diseases in their relation to surgery. It is copiously illustrated and has a good index. R. N.

Syllabus of Lectures on Human Embryology. By WALTER P. MANTON, M. D. Third edition. (*Philadelphia: F. A. Davis & Co., 1906.*)

Outlines of Human Embryology. By GEORGE REESE SATTERLEE, M. A., M. D. (*London: John Wiley & Sons, Chapman & Hall, 1906.*)

When requested several years ago, to review Manton's Syllabus of Lectures on Human Embryology, introductory to the study of Obstetrics and Gynæcology, the book seemed so evidently trivial as to be unworthy of any serious attention. The present review has then been undertaken quite reluctantly.

The book is of small size, comprising about 125 pages, of less than 200 words each. Twenty-five of these pages are devoted to the anatomy of the adult male and female organs, 16 to the chapter headed "Practical Work," 8 to a glossary of terms, and only about 65 to embryology, though an attempt is made to summarize this entire field.

In glancing through the pages, a considerable number of words, found in the glossary for the most part, are seen to stand out in the text in black-faced type or italics. The text more carefully examined, is found to be a sketchy outline of the most conspicuous features of development, bringing in most common terms, yet limiting strictly the information to be gained. The illustrations strengthen this impression. It will be sufficient to refer to the frontispiece of the new edition to indicate our meaning. The section "Practical Work" is equally unsatisfactory, lacking in necessary details, and could hardly be called helpful. Another edition of this work has just appeared and the reviewer is again disappointed at the impossibility of finding anything praiseworthy or worthwhile in it. The original lectures of which the book is a syllabus may be most illuminating, and the book may possibly be useful to the author's own students, but it is difficult to see what further purpose its publication can serve.

Since, however, another author, Dr. Geo. R. Satterlee, has seen fit to issue a similar work and since medical students are so frequently unable to estimate the value of treatises on embryology, or indeed to realize the importance of this fundamental branch of anatomy, we feel obliged to protest against such methods of belittling and condemning a really fascinating subject.

Satterlee's outlines ("A Medical Student's Hand-Book of Embryology") permit more embryology, since 160 pages are entirely devoted to this field, though the matter is not much more extensive than that on Manton's pages. The illustrations are for the most part to be found in McMurrich's "Development of the Human Body"; they are generally much schematized and quite inadequate, the half-tones from the author's photographs adding nothing to the value of the illustrations while they increase the price of the book.

The difficult and fascinating problems of maturation, fertilization, segmentation, and the early formation of the germ-layers are sketched in a very schematic manner within 15 pages, much of which is devoted to pictures and to comparative references to the conditions of development in the lower animals, which would require much more space to be intelligible to a beginner. The chapter which includes the formation of the membranes would be especially unsatisfactory to medical students.

There is no space here for a consideration of each separate chapter of this little book. The subjects are treated in the following manner:

The Alimentary Canal and its Derivatives, 14 pages; Muscles, Extremities, and Skin, 12 pages; Muscular System, 23 pages; Genito-Urinary System, 16 pages; Nervous System, 24 pages; Special Senses, 17 pages; and Glossary, 14 pages. When the small size of the page and the relatively large size and leading of the type and illustrations are taken into consideration, this is certainly a minimal allowance for the treatment, even in outline, of the complicated embryological processes which are discussed.

Such an outline would require special genius for concise and at the same time comprehensive statement to be satisfactory. We regret to say that this book fails to exhibit such characteristics.

It is only within a comparatively recent period that medical students in this country have been expected to be acquainted with embryology and even now the subject receives anything but adequate attention in the medical curriculum. This is not generally true, of course, of the University Medical Schools where some knowledge of comparative embryology is required on entrance, and special study is afterward made of the development of the human body.

Students who have had the advantage of college training in biology, zoölogy, and the embryology of the lower forms will not be attracted to such books as the two here considered. There are, unfortunately, however, a large number of well-meaning medical students who might be induced to spend their money and time on such reading matter, in an honest effort to make up for the deficiencies of their training. We regret to be obliged to say to them that it will be impossible for them to secure, in this way, any adequate conception, or even a glimpse of the facts or problems of the development of the body.

This review is not written to criticise the details of description in these small text-books, nor to find fault with the authors. We feel compelled to protest vigorously, but rather at conditions than individuals.

It seems little short of presumptuous that anyone should deliberately proceed to make this aspect of anatomical science, which has received so many brilliant and capable contributions in this country, ridiculous by attempting to reduce it to such so-called "outlines." How is the student to gain the impression that embryology covers an extensive field full of vital problems and teems with suggestions to aid us in interpreting the form of man? He can here form no conception of the vast amount of work that has been done in this field, nor of the activity that is so evident among the workers of this country. Books of this character belittle the whole subject to such an extent that it seems to be little more than a catalogue of terms. The entire science is thus made to appear capable of being memorized in an evening.

When we find this work done by instructors in our medical schools, we naturally inquire how it was possible for these authors to lose sight of the opportunity to elevate their science and broaden the views of their students, and we are forced to lay the blame at the doors of the institutions where they teach and whose methods have apparently influenced them.

There are still a large number of medical schools which continue to place anatomy on a plane somewhere below practical surgery or medicine and pathology. Admitting its usefulness to these branches they foster its development, however, only in so far as the practical physician dictates, not as an independent science. This attitude has been so general as to be seldom criticised except by a few anatomists, and then at the risk of a snub.

In no other department of science are experts and investigators so constantly dictated to, as to how and what to teach, by others whose work has only a secondary relation to theirs. The surgeon or "practical" physician does not hesitate to dogmatize on how much dissecting, lecturing, quizzing, osteology, neurology, or embryology should be taught by the professor of anatomy.

This generally results in Anatomy, where each course is limited to the demand made by the practitioners. Often there is no real department of anatomy under a scientifically trained man who is devoting all of his time to furthering the development of his science. The obstetrician teaches embryology; the biologists or

pathologists teaches histology and perhaps neurology, if this is not handed over to a clinician; gross anatomy is a lecture course with some demonstrations, or a quiz course in close reference to immediate clinical needs.

Since these are certainly very common conditions under which embryology is taught, is it surprising that its contents may be regarded by many students, and even teachers, as after all of little significance? If such influences are brought to bear on a teacher who has not studied embryology first-hand and from a broad morphological standpoint, it would be remarkable should he produce a more adequate work on embryology. Indeed, he is to be praised for having avoided the pitfalls of verbosity.

H. McE. Knower.

The Vermiform Appendix and its Diseases. By Howard A. Kelly, A. B., M. D., Professor of Gynecology in the Johns Hopkins University, and E. Hurdon, M. D., Assistant in Gynecology in the Johns Hopkins University, Baltimore. With 399 original illustrations, some in color, and 3 lithographic plates. (*Philadelphia and London: W. B. Saunders Company, 1905.*)

In the first section the history of appendicitis is traced through successive stages from the discovery of the lesion in 1759 by Mestivier, to the remarkable work of Fitz in 1886, in which he cleared up the entire subject, both as to diagnosis and treatment.

Then follows an outline of the development of operative technic up to the present time, and the important facts in this very interesting description are emphasized in many places by quotations from the original articles, with brief discussion.

The anatomy of the organ, gross and microscopic, including embryology and comparative anatomy, is carefully considered in a section replete with elaborate and realistic illustrations which do great credit to Mr. Broedel and his associates, and these splendid plates are continued throughout the book, aiding materially the descriptive text.

The chapter on traumatic appendicitis is of interest for the reason that appendicitis is now recognized as being caused by injury much more frequently than formerly.

Attention is called to the fact that "evidence is lacking to show that trauma has caused appendicitis in a previously sound appendix; the presence of a concretion; old adhesions; flexion on itself; cystic condition; unusual shortness and width; being considered as deviations from the normal."

The authors say "one must also bear in mind that the injury need not necessarily be of recent date, although some symptoms, it may be of a vague character, will probably be recalled as immediately following it."

In the other sections the appendix is taken up from every standpoint in a most comprehensive manner, and each chapter covers its subject thoroughly.

The volume is without doubt the most complete and up-to-date work on the appendix and its diseases, and will be welcomed by all physicians and students interested in this important subject, and be of great use to operating surgeons.

Burdett's Hospitals and Charities, 1907. The Year-Book of Philanthropy and Hospital Annual. 18th year. (*London: The Scientific Press, Limited.*)

The value of this publication is recognized by all hospital superintendents and many others interested in philanthropic works, and with each year its importance grows. It is one of the few serials that it is absolutely necessary to students of this branch of social economics. Though it deals in large measure with English institutions, yet, as there is no similar publication in America, the information to be obtained from it is invaluable. R. N.

Biographic Clinics: Influence of Visual Function upon Health. By George M. Gould, M. D. Vols. IV and V. (*Philadelphia: P. Blakiston's Son & Co., 1907.*)

Whether or not the reader agrees with the views propounded by Dr. Gould that many of the minor (?) ills of man are due to disturbances of vision, and that by wearing glasses these ills are cured, and the patient changes from a neurasthenic to a happy, cheerful person, none the less the essays in these two volumes are worth reading. Whatever the cause of the suffering in the men depicted by Dr. Gould may have been, such psychological studies as he has made are interesting, and a closer study of similar morbid conditions, so carefully described by this author, will help any doctor to a better understanding of his patient, and so to a more rational treatment than usually follows a hasty diagnosis of neurasthenia. This is but giving a name to a complex association of symptoms and does not disclose the cause, to which alone treatment can accurately be directed. Dr. Gould has been much laughed at for his views, but his courage in pronouncing them against the generally narrow views of the medical fraternity, who temporarily at least look askance on all novel ideas, and are as narrowminded and slow as any profession in adopting new theories, has had its good result. He has helped to show that more suffering is due to eye-strain than was previously supposed, and if his enthusiasm has led him to maintain views which do not appear on the whole well based, yet the enthusiasm is to be admired, as it has had but good results, and all must respect Dr. Gould for his industry and learning. R. N.

A Manual of the Diseases of Infants and Children. By John Ruhrah, M. D., Baltimore, Md. (*Philadelphia and London: W. B. Saunders Company, 1906.*)

The author in this manual has succeeded admirably in accomplishing the task set forth in the preface, namely, to present the more important facts of pediatrics succinctly to the student and to furnish him with a "rapid reference-book for clinical use." The danger in placing a compendium of any medical subject in the hands of the undergraduate is that, in his study of a disease, he will go no further than to glance at the outlines reviewed in the small volume. This temptation is minimized as much as possible, in the present work, by the frequent insertion of references to comprehensive and recent articles on the more important subjects treated. The opening chapters on the anatomic and physiologic peculiarities of infancy and children, the diseases of the new-born, and infant feeding contain important data found in the larger text-books. In another edition the increasing value of sodium citrate in artificial feeding will doubtless receive recognition. The section on the diseases of nutrition is much too brief to convey to the reader the proportionally large rôle these ailments play in pediatrics. The list of affections of the alimentary tract and chest seems quite complete—though some descriptions, as for example, that of lobar pneumonia are unduly abridged even for a work of this character.

The chapters on the diseases of the skin and infectious diseases are particularly satisfactory, because the nature of these ailments and their differential diagnosis favors terse statement. The frequent association of pavor nocturnus with adenoid growths, and possible partial asphyxia, should be mentioned under disorders of sleep.

A useful chapter on therapeutics is appended, in which the various procedures now used in the treatment of sick children, as well as the most acceptable forms of prescribing the few drugs needed, are carefully stated.

Altogether, the book will prove a valuable quick asset to one who wishes to refresh his memory upon almost any subject belonging to pediatrics.

Human Blood-Vessels. By ARTHUR V. MEIGS, M. D. (*Philadelphia and London: J. B. Lippincott Co., 1907.*)

The book is devoted entirely to the study of the anatomy and pathology of the human blood-vessels, being practically a profusely illustrated record of the changes in the vessels which the author has encountered. It does not profess to be an exhaustive study of the human blood-vessels nor even to be systematic, but is intended to supply the place of the author's previous book on the origin of disease, all unsold copies of which were burnt.

The illustrations, of which there are one hundred and three, are beautifully executed, several of them being exquisite etchings. They are quite objective and, indeed, this is perhaps as well, for the author is in some cases unable to explain the lesion which is represented. In spite of the enormous literature on the subject of the anatomy and pathology of the vessels the author finds it unnecessary to refer to anything except such authorities as the Century Dictionary and one or two text-books.

The text consists of a rambling discussion of the impressions produced by a number of arteries and veins with but little regard for the general principles laid down by others in similar studies. That such isolated work, carried on away from the critical interest of others may lead to error is illustrated in the discussion on pp. 57 and 66. With reference to Figs. 36, 49, and others, where a very local disease of the vein is described and its possible syphilitic origin disputed, it is evident from the drawing that the section had merely passed through a set of valves in the vein, giving rise to the curious appearance.

Other general theories as to the fibroid invasion of vessel walls and other tissues, to the independent new-form also of blood-vessels in the adult, and the intrinsic causes of chronic disease are hardly in accord with the views of most modern pathologists.

Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. New series. No. 25. *On the Importance of Larval Characters in the Classfication of Mosquitoes.* By CAPTAIN S. R. CHRISTOPHERS, M. B., I. M. S. (*Calcutta: Office of the Superintendent of Government Printing, India, 1906.*)

Captain Christophers calls attention to the fact that many writers in describing various genera or species, lay emphasis on characters which are common to all and may scarcely mention the distinctive points peculiar to any given insect.

He describes briefly the features which are common to all larvæ, then in more detail those which are characteristic of many or only a few of the genera. A species of cannibal larva is described which feeds voraciously on younger larvæ and perhaps is a factor in decreasing the number of mosquitoes.

The important variations are found in the forms of ova and their arrangement in rafts—the antennæ, feeding brushes, and papilla of the larvæ, and a few other anatomical structures. The memoir is fully and carefully illustrated. G. H. W.

No. 26. Leucocytozoön Canis. By CAPTAIN S. R. CHRISTOPHERS, M. B., I. M. S.

The parasite has been described by James and by Bentley, who studied it in the circulating blood, but its life history in the organs was not investigated. The writer finds the parasite commonly in dogs about Madras—especially in poorly nourished, neglected animals. The mammalian hemogregarines differ from all forms of blood parasites and their appearance in the dog is very striking. The parasite is found in leucocytes and consists of an oblong, nucleated unpigmented body contained in a capsule or cytocyst, which is probably formed from the substance of the leucocyte. This capsule or cytocyst perhaps explains the difficulty of staining the parasite. The nucleus of the parasite is round or oval and usually situated close to one end. James describes the parasite as invading the polymorphonuclear leucocytes, but the writer calls attention to the fact that the leucocytes which are invaded are decidedly atypical. He concludes from his work that they are immature leucocytes which were infected in the bone-marrow and retarded in development. Such leucocytes show dense nuclear staining—they may retain some motility but to a slight degree only. Motile vermicules are rarely seen in the blood but they can be studied in the gut of ticks which have fed on infected dogs. The bone-marrow shows other forms which are confined to this tissue. Mature cysts are seen which contain at least 30 sporozoits. The cyst wall is thick and hyaline. The sporozoits are of sausage shape and contain a central, irregular, dark-staining chromatin mass. The less mature cysts are exceedingly resistant to stains and are filled with round, clear, refractile granules of large size. They appear to develop from the ordinary encysted form.

One finds in the marrow and rarely in the circulating blood, round or oval naked forms of the parasite, always in mononuclear cells. This is a less mature stage of the parasite in which the cytocyst is not in evidence and the chromatin mass shows differences.

The sexual cycle takes place in the dog tick in the large cells of the gut where conjugation occurs between two similar vermicules. As a result a globular body is formed containing a single large and homogeneous mass of chromatin. This, after three or four days, splits up to form eleven to fourteen sporozoits, which resemble the original vermicules but are thinner. The method of re-entry into the dog is not clear.

The process is true sporogony while the reproduction in the marrow must be considered as schizogony.

The writer reviews briefly the six hemogregarines which have been described. The article is clearly illustrated. G. H. W.

Manual of Anatomy, Systematic and Practical, Including Embryology. By A. M. BUCHANAN, C. M., F. F. P. S., etc., Glasgow. Vol. I, Osteology, Upper Limb; Lower Limb. pp. xvi and 596 + 266 text-figures. Size, 5¾ × 8½ inches. (*Chicago: W. T. Keener & Co., 1906.*)

With commendable frankness the author states that his object has been "to combine a manual of practical anatomy with a text-book of systematic anatomy and so furnish students with a complete treatise on the subject written entirely by himself." (!) He has also aimed "to keep constantly in view the examinational requirements of students." In these words the aim and scope of the manual are well set forth. It is refreshing to find that the author of this carefully done manual, has stated his purpose with such candor for it enables those directing anatomical work to foresee the probable advantages and limitations which the above objects are likely to impose upon any manual of anatomy.

The subject of osteology is treated with clearness and detail. The main variations and the ossification centers of each bone are given with accompanying illustrations for the latter. The illustrations in osteology are fully adequate but occasionally imperfect and in some instances have incomplete legends.

Presumably, in order to avoid repetition, the origins and insertions of the muscles are indicated in these illustrations. Since the muscle attachments are given in red and blue colors they naturally detract somewhat from the value of the illustrations for the purposes of osteology. However, this is a minor matter, if, as is now the custom in our best medical schools, every student is provided with a complete skeleton for home study.

The descriptive text on the anatomy of the upper and lower extremities is an example of judicious condensation. The main facts regarding the muscles are given under the time-honored

headings: Origin, Insertion, Nerve-Supply, Blood-Supply and Action, and a supplementary paragraph is occasionally added on the direction of muscle fibers, etc.

No subject has received undue attention to the exclusion of the rest. The chief facts concerning the lymphatics, nerves, veins, joints, and fasciæ are succinctly stated. All receive as much attention as is possible in a work of this scope. Exceptionally good attention has been paid to the chief arterial anastomoses. The vessels concerned are carefully summarized and usually a good original or selected illustration accompanies the descriptive text. In short, we have here a well-balanced systematic anatomy of small compass.

Following the descriptive text on each extremity, are directions for the dissector. These are explicit and usually follow in such sequence as to permit an orderly exposure of a given area. Since they are separated from the descriptive text which the student would be obliged to consult, it is doubtful whether he would follow them with sufficient care.

Most of the original illustrations are clear and well executed. They show a judicious use of colors, and when in the form of schemes give a clear outline of the related structures. With the exception of Figs. 228, 241, and 242, which lack proportion, and the lymphatic glands as given in Fig. 221, they usually represent anatomical structures faithfully.

We regret exceedingly that the author has practically excluded the B. N. A. from the manual, save as on page 272, where it is used indiscriminately. These, in our opinion, are the main defects. We do find, however, the frequent use of historic names, such as Lisfranc's tubercle, Nelaton's line, Hey's ligament, etc., which we presume answer some of the demands of examinational requirements in Great Britain. It is to be questioned whether the gain to the student in historical perspective through the retention of these names can compensate him for the absence of the accepted anatomical nomenclature of scientific anatomists.

The type is clear, defective letters and words infrequent, and its differential character a great convenience to the student. There is a good index and table of contents and illustrations. We should like to include the word "dry" as applied to the skeleton and the expression "axis spine" among typographical errors.

The paper is of good quality and the binding in flexible covers and English Buchram especially well chosen. The price is reasonable. S. W. M.

Diagnostic Methods. By Prof. Hermann Sahli. Being an authorized translation of the fourth (last) German edition, by F. P. Kinnicutt and N. B. Potter. 8 vo., 1008 pages, numerous illustrations. (*Philadelphia and London. W. B. Sanders Company, 1905.*)

In giving to the profession an English translation of Prof. Sahli's great work, Drs. Kinnicutt and Potter have put us under a real obligation.

Comprising as it does a careful and exhaustive treatise on all the methods, physical and chemical, which are used in medicine, including the special branches, the work is an invaluable source of help to the student and practitioner.

Since its first appearance in 1894, the work has gone through several editions and enlargements and embodies not only a full and critical presentation of current methods and opinions but also a great deal of new matter, the result of investigations by the author, his assistants, and pupils. It is, therefore, not merely a compilation but a contribution to the advancement of medical science.

The sections on physical diagnosis, and those on gastric and urinary diagnosis are particularly worthy of note. In fact, of works covering the whole field of method there is none which is so good.

The American translators have done their work well and have added a number of illustrations and comments of value.

T. R. B.

Practical Dietetics with Reference to Diet in Disease. By Alida Frances Potter, Graduate, Department of Household Arts, State Normal School, Framingham, Mass., etc. Fourth edition. (*New York: A. F. Potter, Publisher.*)

This book has received unusual commendation from the fact that it has been adopted by the medical department of the U. S. Government, also by the Canadian Government in its schools of instruction for the militia, and has been authorized as a textbook in the New York public schools. In many respects it well deserves these marks of appreciation, but the reviewer feels that before another edition is printed, the work needs very careful revision. In his opinion the best part of the book is the portion devoted to receipts; these are well chosen and simple. Miss Potter uses a "speck" as a measure about equal to ⅛ of a teaspoon,—the old-fashioned "pinch" would seem to be a better word to use, though perhaps quite as inaccurate in exact measurement. Proprietary names of foods should be discarded from such a work; example, Welch's Grape Juice, Horlick's Malted Milk, and others. "Sweetina" should give way to saccharine.

The introductory chapter on digestion could be made clearer were it more simple, and did it not attempt to give in brief form information which cannot be well condensed. The directions for disinfecting utensils are not satisfactory, and the tables of exact equivalents in weights, and for preparing percentage solutions might be omitted.

Miss Potter should eliminate the word "dainty" from her vocabulary, as its frequent recurrence is distasteful. A soup can never be "dainty." The following sentence in the chapter on fruits is perhaps the worst in the book, and should not have been allowed to pass through four editions: the expurgative fluid reaches every part of the system, rinsing out morbid humors, and restoring congestive (!) organs to a healthy state of functional activity. "Pressure on the lungs" for "oppression," also needs correction, and the statement that bananas act as a "stimulant to the nerves" is one that cannot pass unchallenged.

The book has much merit, but the use of the proprietary names of foods diminishes its value and our estimate of it is lowered. We cannot recommend its use until it has been purged of all advertisements. R. N.

Twentieth Annual Report of the State Board of Health of the State of Ohio, for the Year ending December 31, 1905. (*The Springfield Publishing Company, Springfield, Ohio, 1906.*)

This report of nearly 500 pages is interesting and valuable. It demonstrates the good work being done by the State along lines of public hygiene, of which the best proof is the annually diminishing death rate throughout the State. Two-thirds of the report is taken up with papers relating to water supplies and their purification, and the proper disposal of sewage. It is to be greatly desired that the question of tuberculosis should hereafter receive more attention. With the exception of diseases of the nervous system, which, with 4213 deaths, lead the list of diseases in the mortality reported for the year, pulmonary tuberculosis takes second place with 3935 deaths. Doubtless many more died of this disease, but their deaths have been recorded under other heads. This is more than three times the number of those who died from typhoid fever. It is satisfactory to note that but very few deaths, 76, are attributed to malaria, thus showing that the doctors far and wide, are no longer attributing to this disease, as they have done in the past, many obscure forms of death.

It is a proof of the value of persistent and prolonged education along certain definite lines. The health of the United States depends in large measure on the high education of its doctors, and every well-learned lesson of this nature will help to improve the general welfare. R. N.

Text-Book of Midwifery for Nurses. By ROBERT JARDINE, M. D., Edin., etc. Third edition. (*London: Henry Kempton; Chicago: W. T. Keener & Co.*)

This is a compact little volume dealing with the practical side of obstetrics. It is very clearly written and would seem well adopted to the needs of nurses, for whom it is intended. The illustrations are few but well chosen.

The Diseases of Women. By J. BLAND-SUTTON, F. R. C. S., Eng., and A. C. GILES, M. D., etc. Fifth edition. (*New York: Rebman Co., 1896.*)

That this little volume has entered its fifth edition proves that it has met a need, and it is deservedly popular.

The authors emphasize their endeavor to keep the book in as small a volume as is possible, and they have succeeded admirably. In this small volume every unusual and diseased condition of the reproductive organs of women finds a place, the authors devoting some space to the anomalies due to arrest of development, as as well as to the normal development, anatomy, and physiology of these organs.

Puberty, menstruation and its irregularities, and the menopause are given due consideration; a very welcome addition to a text-book of this character.

A novel departure is the section devoted to the vaginal secretions, both normal and pathological, with an enumeration of the causes, and a graphic description of the physical characteristics of each. There is a long list of the bacteriological findings in the vaginal secretions, given, perhaps, in the order of their frequency, if not in that of their relative importance. The gonococcus of Neisser is placed (5th) fifth in the list, instead of (1st) first, where experience would indicate it belonged, and where the authors practically admit it, in the third paragraph on page 125, and again in section C on page 130. Many of the organisms on the list are rarely seen in practice, and must be classed as belonging to some of the gynæcological curiosities, in which the book abounds. For this wealth of information alone, *i. e.*, reports of the unusual conditions met, the book is well worth the reading.

The descriptions of conditions are clear and concise, and the treatment on the whole conservative and rational, though much of the technique of both treatment and operation had to be sacrificed in the condensation of the volume, which is to be regretted in a text-book for students.

In but two points, the operations as advised, seem not to be up to modern requirement: First, in the repair of perineal lacerations, the old method is continued, instead of the union of the torn muscles, which would seem the logical aim of the operation; and, again, in inoperable cysts of the ovary, the authors advise uniting the edges of the cyst, to the edges of the abdominal wall, even at the risk of the patients dying a miserable death from exhaustion, due to suppuration (page 496). This would not appeal to one as good surgery, even though we realized that the patient would probably die anyhow, it seems cruel to inflict upon a dying patient the constant and painful evidences of her hopeless condition.

As before said, the book deserves its popularity even in spite of the criticism above made. It is well written, both the paper and type are attractive, and the illustrations, though mainly diagrammatic, serve the purpose for which they are intended. If we may use the simile, the book appears "a bird's-eye view" of the field of the diseases of the reproductive organs of women.

Cook County Hospital Reports, 1906. Compiled and Edited under the Direction of the Publication Committee of the Cook County Hospital Staff. (*Chicago: The Henry O. Shepard Co., Printers, 1906.*)

This volume is to be welcomed as an index of the spirit of the men who have produced it. The introduction begins thus: "Through the developments and reorganizations of recent years and the co-operation of its medical staff a new, modern hospital has been presented to Cook County, and this little volume is an earnest pledge of the permanency of the gift. The old county institution, reborn and clothed in modern garb, is destined to take a dignified position in the galaxy of real hospitals, whose functions extend infinitely further than to the mere taking care of the indigent poor. Hereafter, it is hoped, it will join with the Johns Hopkins, Massachusetts General, and others of that type in the pursuit of original research, to develop the medical knowledge of the world." The pledge the staff has taken has been well kept, and there is no doubt that in their earnest endeavor to attain the standards set by the hospitals they name, they will in due time produce work as good as that done elsewhere. The hospital has an evil past history, that must be blotted out, and if the present staff do not get dispirited, they can make the hospital one of the notable landmarks of the country. The thirty-six papers in this volume deal with a number of persistently interesting topics to all students of medicine and surgery in their multifold specialties. It is a worthy addition to the already long list of hospital reports. R. N.

Tumors of the Cerebrum: Their Focal Diagnosis and Surgical Treatment. By CHARLES K. MILLS, M. D., and others. (*Philadelphia: On sale by Edward Pinnock, 1906.*)

This volume is composed of seven articles, five of which are reprints from the University of Pennsylvania Medical Bulletin for the year 1906; the remaining two have not apparently been published elsewhere, but have been read before societies. All the authors are Philadelphians, so that the volume is valuable as presenting the views of a group of men who are already well known for their admirable work in neurology. Each paper deserves careful study, and the volume as a whole is an important contribution to the literature of these special tumors, which still offer so many difficulties in their correct diagnosis and treatment both to physicians and surgeons. R. N.

ERRATA.

BENJAMIN RUSH, AS MATERIALIST AND REALIST.

By I. WOODBRIDGE RILEY, PH.D.,

(THE JOHNS HOPKINS HOSPITAL BULLETIN, *March, 1907.*)

Page 91, 1st column, 4th line from bottom, for Shaftsbury read *Shaftesbury.*

Page 92, 2d column, 19th line from top, for quiddites read *quiddities.*

Page 101, 1st column, 1st line from top, insert *he* after *could.*

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THE SUTURE OF BLOOD VESSELS. IMPLANTATION AND TRANSPLANTATION OF VESSELS AND ORGANS. AN HISTORICAL AND EXPERIMENTAL STUDY.[1]

By Stephen H. Watts, M. D.,

Assistant Resident Surgeon, The Johns Hopkins Hospital.

It is only in comparatively recent years that conservative methods have been employed in dealing with the larger blood vessels in the human body. This advance is in a large measure due to the results obtained by the application of modern surgical technic to animal experimentation.

The ligature, which during the middle ages waged a constant warfare with cauterization, compression and other methods of hæmostasis, was toward the end of the eighteenth century recognized as the best method for controlling hæmorrhage from large and small blood vessels. Inasmuch as ligation of the large vessels not infrequently gave rise to gangrene and sometimes caused loss of life, this method was not an ideal one. Some years elapsed, however, before further progress was made; then surgeons began to apply the lateral ligature in partial wounds of veins where the continuity of the vessel was not interrupted. This method was first used successfully about the beginning of the nineteenth century (1), but, as was the case in other branches of surgery, first came into general use after the introduction of antiseptics. The lateral ligature has the disadvantage that it can be used in only a limited number of cases, for if the wound in the vessel is large the ligature will produce considerable narrowing of its lumen and there is danger of the ligature slipping. To meet these difficulties various clamps were devised for approximating the edges of venous wounds during the process of healing, but the great objection to this method, although it was a step in the right direction, was that it prevented primary healing of the cutaneous wound.

The Lateral Suture of Veins and Arteries.

The problem was solved by the introduction of the venous suture, which was carried out for the first time successfully by Schede (2) in 1882. This method was later employed in numerous cases and has now come into such general use that almost every surgeon of experience has had occasion to use it.

The beginning of a conservative treatment of arterial wounds antedates by more than a century the first experiments with the lateral suture of veins. In 1759 Hallowell, an English surgeon, at the suggestion of Lambert (3), who had observed the spontaneous healing of vessel wounds after venesection, sutured an artery in man for the first time. A small wound in the brachial artery was closed by placing a pin through the lips of the wound and passing a thread around it. The patient recovered and the radial pulse remained nearly as strong as that in the other arm.

In 1772 the question of arterial suture was tested experimentally by Asman (4), who closed wounds in the femoral arteries of four dogs by the same method which Hallowell had employed in man. None of these experiments were successful, and Asman therefore declared the method insecure and

[1] From the Hunterian Laboratory of Experimental Medicine, The Johns Hopkins University.

dangerous. It was not until 1881, after antisepsis had gained a firm foothold, that arterial suture was again tried in animals, but without the desired result. In 19 cases Gluck (5) sutured longitudinal wounds in the common iliac arteries of large dogs and in the aorta of rabbits, but there was always hæmorrhage from the stitch holes and in tying the sutures tears were often made in the vessel wall. To overcome these difficulties he later constructed small ivory clamps, with which the wound in the artery was closed and which were allowed to remain in situ. In this manner he succeeded in closing a partial wound of an artery with preservation of its lumen. Several years later v. Horoch (6) experimented with arterial suture, but, likewise, with little success.

To Jassinowsky (7), who published the results of his experiments in 1889 in his inaugural dissertation, belongs the credit of having proven conclusively that arterial wounds can be sutured with preservation of the lumen of the vessel. He avoided the femoral artery, which had been used by previous experimenters, and used the carotids of large dogs, horses, and calves, making longitudinal and transverse wounds in the vessels and then suturing them. The longitudinal wounds varied in length from 3 mm. to 2 cm. and the transverse wounds included $\frac{1}{4}$ to $\frac{1}{2}$ of the circumference of the vessel. Of 26 experiments, all were successful except four, and in none of the successful cases was there secondary hæmorrhage, thrombosis or aneurysm formation, although some of the specimens were examined as late as a hundred days after the operation.

Histological examination of the old scars showed the following condition: There was a small gap in the elastic membrane at the site of the suture, the ends of the membrane being usually slightly everted, leaving a small angle, filled with fibrous connective tissue, which toward the lumen was covered with endothelium. The media showed an increase in its cellular elements, and there was an irregular arrangement of the elastic lamellæ and muscle cells, the nuclei of the latter being quite large. The adventitia was greatly thickened consisting of a fibrous connective tissue poor in cells.

Jassinowsky attributed his good results to his technic and to the fact that he experimented upon vessels of large caliber. He used fine curved needles and fine silk, the interrupted sutures being placed about 1 mm. apart, including only the media and adventitia and avoiding the intima. As a result of his experiments he reached the following conclusions: (a) The arterial suture heals by first intention; (b) bleeding after operation can be surely and completely avoided; (c) secondary hæmorrhage and thrombosis are not to be feared; (d) suture should be done in all recent, clean longitudinal, oblique, and flap wounds of large vessels and in transverse wounds not exceeding one-half the circumference of the vessel; (e) the strictest asepsis is necessary; (f) the suture is easily done.

In 1890 Burci (8), by experiments on the femoral and carotid arteries of dogs and horses, confirmed the results obtained by Jassinowsky. Of six experiments four were said to have been successful. He used fine round needles and a continuous silk suture, only the adventitia and media being included in the suture.

In the summer of 1894 Heidenhain (9) made several experiments upon the carotid and femoral arteries of dogs, suturing partial wounds in these vessels with a continuous catgut suture, approximating intima to intima. None of these experiments were successful; hæmostasis was perfect but the lumen was occluded by the suture. He attributed his failure to the small caliber of the vessels and the coarseness of his suture.

Murphy (10) in 1897 published the results of numerous experiments with the partial suture of arteries along with other experiments with the resection of arteries.[2] He sutured 11 partial wounds in the abdominal aorta, carotid, femoral and iliac arteries of dogs and two wounds in the carotids of sheep. These were longitudinal and oblique wounds $\frac{1}{4}$ to $\frac{3}{4}$ inch in length and transverse wounds including $\frac{1}{3}$ of the circumference of the vessel. Of the 13 sutures 6 were entirely successful, the lumen of the vessels being preserved. In 10 cases a continuous suture of fine silk, including all the coats of the vessel, was used; in one, interrupted silk sutures were used, and in two, kangaroo tendon was the suture material. As the means of provisional hæmostasis Billroth clamps armed with rubber were usually used, sometimes a heavy silk thread twisted and held with the fingers.

As a result of his own and the experiments of others Murphy came to the following conclusions: (a) Besides the most careful asepis, a good technic is necessary for the success of vessel suture; (b) the vessel must be exposed very carefully and a good means of provisional hæmostasis applied; (c) the edges of the wounds must be accurately approximated and bleeding completely stopped; (d) as suture material he recommends silk which should include only the outer coats of the vessel; (e) he recommends the suture of the vessel sheaths and surrounding tissues as a support to the vessel suture.

In 1897 and 1898 Silberberg (11) experimented with the arterial suture in dogs. He applied 12 longitudinal and 6 transverse sutures, 10 in the femorals, 6 in the common carotids, and 2 in the abdominal aorta. Five of the longitudinal and 3 of the transverse sutures were quite successful. For a successful suture Silberberg emphasized the importance of an absolute asepsis. As suture materials he used the finest Hagedorn intestinal needles and the finest silk. With the exception of three cases in which he used interrupted sutures, he made use of the continuous suture, which can be applied more rapidly. He does not attach much importance to the question as to whether the suture should or should not penetrate the intima, but thinks that sutures exposed in the lumen may contribute to thrombus formation. He thought a method of provisional hæmostasis, which spares the vessel wall as much as possible, was very important and made use of heavy silk threads which were passed around the vessel and,

[2] Vid. infra.

after being twisted, were held thus by means of clamps. The slight bleeding from the stitch holes is easily stopped by a little compression. As an additional support he recommends the suture of the vessel sheath. Concerning the indications for vessel suture this author says: (a) The wound should be clean; (b) only large vessels, such as the aorta, the carotid, subclavian, axillary and femoral vessels, should be sutured; (c) longitudinal, oblique, and transverse wounds, which do not exceed one-third of the circumference of the vessel, are adapted to suture.

Napalkow (12) in 1900 reported the results of his experiments with the suture of wounds in the heart, arteries, and veins. Of 14 sutures in the abdominal aorta and carotids of dogs, in six there was bleeding at the site of the suture. Of 10 venous sutures only one bled. Napalkow used fine round needles and continuous sutures of fine silk, including all the coats of the vessel. As the means of temporary hæmostasis he employed a thread twisted about the vessel or clamps armed with rubber.

In 1899 Dörfler (13) published a very interesting and instructive paper, describing the results of his experiments with the suture of arteries. Altogether there were 20 experiments, 16 being simple sutures of longitudinal, oblique and transverse arterial wounds with 12 successful results and 4 being sutures of completely divided arteries, which will be described later.[3] As the result of his experiments, Dörfler came to the following conclusions: (a) Arterial suture is only indicated in clean wounds; (b) for temporary hæmostasis the best means are compression with the fingers, strips of gauze twisted together, or clamps armed with rubber; (c) fine needles and a continuous suture of fine silk including all the coats of the vessel should be used; (d) slight pressure upon the suture for a few minutes after its completion will readily stop bleeding; (e) the vessel sheath should also be sutured.

Jakobsthal (14), who examined Dörfler's specimens histologically, found that the process of healing of arterial wounds proceeds as follows: The incision becomes filled with blood and fibrin, there being only slight deposits within the lumen about the suture and upon the inner aspect of the vessel wound. These deposits are very early, even in the first few days, covered with endothelium. Soon there is an active formation of new connective tissue and blood vessels in the adventitia and to a lesser extent in the media. These make their way into the clot and in a certain measure organize it, thus forming an end-, mes-, and peri-arteritic growth rich in cells. Then there is a retrogressive process; the cells become fewer and less rich in protoplasm, while a fibrous substance appears between them. This substance in the media and adventitia is chiefly connective tissue with a few elastic elements, while in the intima there is an extraordinarily rich new formation of fine elastic lamellæ and fibers which may lead to the formation of a kind of secondary elastica, at least in the region of the scar.

Salvia (15) in 1902 experimented upon dogs, goats, and a donkey in order to study the process of healing arterial wounds. He partially divided the vessels and closed the wounds with interrupted sutures. He found that, with the exception of the elastic fibers, there is a complete restitution of the vessel wall.

In 1906 Dorrance (16) published a method of vessel suture, which he claimed to be original with him, but which is almost identical with that described by Clermont (17) in 1901. Dorrance used a continuous mattress suture of fine Pagenstecker's thread with the dropping-back one-half a suture length every third suture, continuing the same suture as a whip-stitch over the everted edges of the artery after completing the mattress suture. With this method he experimented with the closure of wounds in arteries and the union of completely divided arteries.

There were 14 operations in all, nine on horses and five on dogs, and of the 14 wounds 12 suppurated. There were three complete circular and 11 partial transverse, oblique and longitudinal wounds. Ten of the vessels were examined from 2 to 14 days, and the other four from 21 to 42 days after the operation. In seven no thrombus was visible, in five a small mural thrombus was present and in two complete thrombosis. These are remarkably good results considering the number of suppurations. I am inclined to think that, had the specimens been examined at longer intervals after operation, more complete thromboses would have been present, especially when we consider the number of cases in which mural thrombi occurred.

While animal experimentation has shown conclusively that arterial wounds can be sutured successfully, numerous instances of successful suture of accidental wounds of arteries in man have demonstrated the practical value of this procedure. Such cases have been reported by Heidenhain (18), Israel (19), Ssabanejew (20), Orlow (21), Lindner (22), Garré (23), Seggel (24), Veau (25), Heinlein (26), Baum (27), Torrence (28), and others. Up to July, 1902, Schmitz (29), was able to collect 21 cases of lateral sutures of arteries in man, the axillary artery having been sutured seven times, the femoral five times, the popliteal and brachial each three times, the common iliac, common carotid, and internal carotid each once. In 1903 Höpfner (30) collected 30 such cases.

Remarks.—The results of the foregoing experiments on animals and the clinical experience show that for a successful suture the following things are necessary: (a) A very perfect aseptic technic; (b) clean cut wound edges which can be approximated without too much tension; (c) very careful handling of the vessel without stripping its sheath too much.

While there is considerable difference of opinion as to whether silk or catgut is the best suture material, there is little doubt that the former is preferable. It can be obtained in finer sizes, handled much more easily, and sterilized more surely. The needles should be as fine as possible, but whether straight or curved depends upon the location of the vessel to be sutured.

The question as to whether the interrupted or continuous

[3] Vid. infra.

suture should be used, seems to be settled in favor of the latter, which is simpler and can be applied more rapidly. The question as to whether the suture should penetrate all the coats of the vessel or avoid the intima, seems of more importance. While Jassinowsky (7), Burci (8), and others recommend the avoidance of the intima, v. Haroch (6), Murphy (10), Dörfler (13), Dorrance (16), and others allow their sutures to penetrate the intima, in fact, in suturing veins it is almost impossible to avoid it. By including all the vessel coats the suture is not only simplified, but made more secure.

Various methods have been used for producing temporary hæmostasis, finger pressure, various clamps, strips of gauze, etc. Whatever method is employed, the main desideratum is to injure the vessel wall as little as possible. The pressure of the fingers is the gentlest method and should be used in man, where possible.

If there is leakage at the site of suture a slight compression will generally cause it to cease in a few minutes.

The Circular Suture of Arteries and Veins.

Inasmuch as the lateral suture was not successful in large transverse wounds of vessels and in cases where the edges of the wound were crushed or otherwise injured, attempts were made in such cases after resection of the vessels, and in complete transverse wounds of vessels, to unite the ends of the vessel by the simple circular suture, by protheses of various kinds or by invaginating one end into the other.

The circular suture of arteries.—The first experiments of this nature were those of Robert Abbe (31) of New York, who published his results in 1894. He divided the femoral artery of a dog and united it again by tying the ends together over a small hourglass-shaped tube of thin glass. The immediate result of the operation was very favorable, for the circulation of the leg was reestablished as soon as the clamps were removed and the dog recovered promptly. After some time the artery was removed and examined. The tube was found lying free in the lumen of the vessel which had become occluded a short distance below it. Abbe united the divided aorta of a cat in a similar manner and afterwards exhibited the animal, thinking that its survival demonstrated the patency of the aorta. This vessel, however, might have become gradually occluded without inconvenience to the animal.

In 1896 Briau and Jaboulay (32) made ten experiments with the circular suture of carotid arteries in dogs, the ends of the vessels being united with U-shaped sutures, which everted the edges and approximated intima to intima. None of the experiments were successful, all of the vessels becoming thrombosed. They later tried the method on a larger vessel, namely the carotid of a donkey, with perfect success. This method was tried in 1900 by Salomoni (33), who claimed the honor of discovering it.

Murphy (10) in 1897 published a very interesting and important article in which he detailed his numerous experiments with the suture of arteries and described a new method for the union of completely divided vessels. This method, which is said to give a more solid union than the simple suture, consists in invaginating one end of the vessel a short distance into the other and is done in the following way: After applying Billroth clamps armed with rubber, the artery is divided and the proximal end is invaginated into the distal by means of three or four double-needled silk sutures which include only the adventitia and media of the proximal end, but are passed through the entire thickness of the distal end. When these sutures are drawn up and tied the ends are easily invaginated and fastened in this position. After the invagination is completed, the free edge of the distal end is sutured to the proximal by several interrupted sutures which include only the adventitia and media of the proximal end, but the entire thickness of the distal. The invagination is sometimes facilitated by splitting the distal stump longitudinally for a short distance.

This method was tried on the carotids of dogs three times, on the carotids of calves four times and on the carotids of sheep four times, once on the femoral artery and abdominal aorta of dogs. Only three of these cases were successful, thrombosis occurring in the others. The unfavorable results were thought to be due in a large measure to the small caliber of the vessels which were used.

Murphy also made a few experiments with the simple suture of arteries, the carotids of sheep being sutured twice, the carotids of dogs and calves once each and the abdominal aorta of a dog once. The continuous suture was used four times and the interrupted suture once. Only one of the five experiments was successful.

The invagination method was tried by Dörfler (13) four times, twice in the carotids and twice in the femorals of dogs. In three cases thrombosis occurred; in the other case the lumen was unobstructed when the animal died of a venous hæmorrhage only three days after the operation.

In discussing Murphy's paper at the International Medical Congress in Moscow in 1897 Nitze (34) demonstrated some small ivory protheses, resembling those later described by Payr. They consist of small ivory cylinders over which the ends of the vessel are slipped in such a way as to approximate intima to intima. A simple ligature holds them in this position.

In 1898 Gluck (35), who had done pioneer work with the lateral suture of arteries, described a new method of circular suture. After exposing the artery and applying clamps armed with rubber, a small section of the artery was excised and slipped over one of the ends in the manner of a cuff; the ends of the vessel were sutured together with interrupted sutures which included only the adventitia and media, and then the resected portion was drawn over the line of suture and fastened thus with a few stitches. Instead of using a section of the artery to be sutured, rings of rubber and decalcified bone or a section of vessel from the same or another animal can be used.

Payr (36), fearing that a simple circular suture could not withstand the pressure within large arteries devised a method,

which he published in 1900, of uniting divided vessels by invaginating the ends over extra-vasal protheses of magnesium, which is absorbable in the body. If the vessel is an artery, the central end is invaginated into the peripheral, if a vein, the peripheral end is invaginated into the central. The protheses consist of hollow cylinders of magnesium, which have very thin walls and vary from .3 to 1 cm. in length. On the outer surface of the cylinder, near one end, there is a small groove, one-third to two-thirds of a millimeter deep, in which the ligature is placed. The method, as applied to arteries, is carried out as follows: After provisional closure and division of the artery, the central end is drawn through the cylinder, which just fits over the vessel, by means of three sutures placed in the end of the vessel, which, after being drawn through the cylinder, is everted over it and fastened thus with a ligature of fine silk. The peripheral end is then drawn over the everted cuff and also fastened with a ligature, broad surfaces of endothelium being thus approximated. Payr thinks the fact that the prothesis is absorbable is of great importance. This property of the prothesis is probably of very little importance, for it requires from two to four weeks, or even longer, to be completely absorbed.

Payr, who tried the method on the carotids of dogs and pigs, says it can be done very easily and quickly and claims to have obtained very good results with it; however he does not state how many experiments he has made and makes no reference to any journal of experiments. The article is illustrated with schematic drawings, all of his preparations having been destroyed in a fire.

In an article published in 1904 Payr (37), on the strength of the experiments of others with it, notably those of Höpfner (38), champions his method and says the unsuccessful experiments of Salinari and Virdia (39), Jensen (40), and Reinsholm (41) were due to the fact that they did not proceed according to his directions.

In 1901 Bouglé (42) performed a few experiments with circular suture of the carotids of dogs. He first used the method of Murphy, invaginating the ends by means of U-shaped sutures. The vessels, however, were so small that obliteration of the lumen always occurred. He then tried a new method, invaginating the ends only a few mm. and fastening them thus by interrupted sutures, which included only the media and adventitia. He mentions one case, in which both carotids were sutured, one by this method, the other by simple end to end union with interrupted sutures which did not include the intima. When examined 15 days after operation both vessels were patent, the intima was smooth and no clots were present.

In 1902 articles upon the circular suture of arteries by Salvia (43), Salinari and Virdia (39), Carrel (44), Thomaselli (45), and others appeared.

Salvia (43) made numerous experiments upon the femorals of dogs and the carotids of donkeys and sheep with special reference to the process of healing in wounds of arteries. He employed the end to end suture with fine silk, after resecting considerable lengths of the vessels. In none of the cases did the lumen remain patent. He examined the specimens histologically and found that, with the exception of the elastic fibers, there was a complete restitution of the vessel wall.

The object of the experiments of Salinari and Virdia (39) was: (a) To test the methods most often tried in animals and man and from the results to determine which offers the best chance of restoring the function of the vessel; (b) to investigate the healing process microscopically and see whether the arterial walls will be sufficiently strong at the sutured point. The experiments, about 30 in number, were done on large dogs, the carotid and femoral arteries being generally used, the abdominal aorta being used twice. With the exception of a few partial transverse and longitudinal sutures, the sutures were done on completely divided arteries. For provisional hæmostasis various clamps were used, but, finding these unsatisfactory, they constructed a special clamp with parallel blades, regulated by a thumb screw, which proved very satisfactory.

Of 16 sutures done according to Murphy's method, six became infected and the results were negative, six healed with mural or canalized thrombi; in two the lumen remained pervious, though considerably narrowed, and in two others the site of suture presented an almost normal appearance. The protheses of Payr were tried three times, two of the animals died of infection, the other of secondary hæmorrhage.

The authors conclude that suture is preferable to ligation in wounds of large size and that in cases of complete transverse wounds invagination is the best method, although their results would hardly justify these conclusions. In cases of *restitutio ad integrum* the vessel wall is richer in muscle cells and elastic fibers than under normal conditions.

Thomaselli (45) emphasized the importance of approximating intima to intima. In his experiments, which were done on the abdominal aorta, carotid and femoral arteries of 11 dogs and the femoral artery of one goat, the endothelial surfaces were held approximated by fine clamps, which were removed in turn as the suture proceeded. Interrupted sutures, passing through all the coats of the vessel were used and the suture materials were fine curved needles and silk thread. In seven cases there were positive results with or without narrowing of the lumen, in three the results were negative and in two others it was necessary to ligate on account of sclerosis of the vessel wall.

In an article published a year later Thomaselli (46) says, that the best method of vessel suture is that previously recommended by Salomoni (33), which consists in approximating intima to intima by means of U-shaped sutures transfixing the entire wall of the vessel. He studied the process of healing in transverse wounds to determine whether there is a real *restitutio ad integrum* as Burci had already observed in the case of longitudinal wounds. Histological examination showed the following: (a) The muscular layer is completely regenerated; (b) the elastic fibers of this layer are regenerated and are more numerous at the edges of the scar and near the lumen where they do not form a real inner elastic

membrane, but they replace this membrane and prevent the formation of an aneurysm; (c) neither the inner elastic membrane nor the elastic fibers of the adventita are reformed, the latter being composed of fibrous connective tissue; (d) close up to the suture one can demonstrate the complete restoration of the three layers with hypertrophy of the muscle cells and elastic fibers.

In 1902 Carrel (44) published a method of circular suture, which, while differing very little from certain methods previously employed, has greatly facilitated such sutures. The ends of the vessel to be sutured are first united by three tension sutures of fine silk, inserted at equidistant points on its circumference. Traction upon these sutures approximates the edges of the vessel and renders the application of a continuous suture comparatively easy. In his original communication Carrel recommended avoiding the intima, where possible, but in his later experiments the sutures have included the entire thickness of the vessel wall. He has made no systematic study of the circular suture of divided arteries and veins but by applying his method to arterio-venous anastomoses and the transplantation of vessels and organs has obtained brilliant results.[4]

In 1903 an article by Jensen (40) on the circular suture of blood vessels, which was awarded a gold medal by the University of Copenhagen, was published. In this very complete and interesting article Jensen describes the various methods for uniting completely divided vessels which had been used up to that time and gives a critical review of the results obtained with them. Jensen's own experiments in which bone protheses, the magnesium protheses of Payr, and the various suture methods were tried on the vessels—mostly the internal jugular veins and carotid arteries—of horses and goats, were undertaken with a view to solving the following questions: (a) Why does thrombosis occur so often? (b) in how far does this or that method offer a better guarantee against thrombus formation?

Of three arteries united by Murphy's method two became completely thrombosed and one remained unobstructed; of three united by invagination over protheses of bone, in two the lumen was much narrowed and in the other almost obliterated; of twelve united by sutures seven were thrombosed, three were more or less constricted, and two were neither thrombosed nor constricted.

Ten veins were united by various protheses; of these eight became completely occluded and two remained patent but partly occluded. Seven veins were united by sutures; of these four were thrombosed, two more or less constricted and one neither thrombosed nor constricted.

From these results which are not very encouraging, Jensen rejects protheses and concludes that the best method of uniting completely divided vessels is to insert two or three simple interrupted or U-shaped sutures and join them by continuous sutures. He prefers silk to catgut and allows the suture to include the entire thickness of the vessel wall. He thinks thrombosis is due chiefly to infection with pathogenic organisms and says, "If we accept infection as the only cause of thrombus formation we have the best explanation of the capriciousness of the results of the experiments. This agrees also with the fact that sutures not involving the intima are more likely to succeed, for infection of the lumen is more difficult if the suture does not enter it."

In an extensive article published in 1903 Höpfner (30) gives statistics of the results of the ligation of large arteries and veins in man and thus points out the need of a practical method for uniting completely divided vessels. He then gives a history of the lateral and circular suture of vessels in animals and man. He experimented with the circular suture of vessels, vessel implantation and transplantation, and the replantation of amputated extremities, using the magnesium protheses of Payr.

Of six arteries united by this method, two became thrombosed and four remained unobstructed, three of these being examined eight days after operation and one four weeks after operation. The experiments with transplantation and implantation of vessels and the replantation of amputated extremities will be described later.

In 1903 Amberg (47) experimented with the circular suture of arteries in horses and large dogs, using the carotids, femorals, and abdominal aorta. After dividing the arteries, the ends were split longitudinally for a distance of 3 to 4 mm. so that the edges could be everted after the manner of flanges which were then sutured together intima to intima. His experiments were not very successful, for in only three of the six cases was the lumen entirely preserved. In one there was a mural thrombus and in the remaining two complete thrombosis and secondary hæmorrhage occurred.

Hubbard (48) in 1903 made several experiments with the lateral and termino-lateral anastomosis of the carotids of dogs. Of eight anastomoses all were thrombosed except two, and in these the lumen was almost completely obliterated.

In 1903 De Gaetano (49) tried on dogs a new method for the transverse suture of arteries. He placed a small spindle-shaped glass bobbin in the lumen of the vessel and applied the suture over the bobbin which was removed when the suture was nearly completed. This is said to greatly facilitate the suture. I have not been able to consult the original article and therefore cannot give the results of the individual experiments. According to De Gaetano histological examination of the specimens four months after suture showed a complete restitution of all of the elements of the vessel wall, including the elastic fibers.

In an article published in 1903 Reinsholm (41) presents an exhaustive study of the various methods for uniting large blood vessels and then gives the results of his own experiments with these methods. He thinks union with sutures is the best method and that the sutures, which should be of catgut, should not include the intima but a sufficiently firm portion of the vessel wall. I am sorry that I have been unable to consult his original article.

[4] Vid. infra.

In an article published in 1903 Chérie-Lignière (50) reviews the various methods of arterial suture and concludes that the simple suture is only applicable to longitudinal wounds and not to transverse wounds. He describes the Payr method in detail and reports his own experiments with this method. Of six cases in which the arteries of dogs and donkeys were thus united, in four the results were good, in two there was secondary hæmorrhage, once due to necrosis, once to infection. The magnesium cylinders were absorbed in 20 days. Secondary hæmorrhage is prevented by strict asepsis and the isolation of only a short stretch of vessel.

In 1903 Lejars (51) recommends the suture in longitudinal wounds of large arteries provided the operative field is aseptic, but if more than one-half the circumference is divided he thinks ligation is advisable, for after suture in such cases narrowing of the vessel lumen, secondary hæmorrhage, and sometimes peripheral embolism is to be feared.

According to Garré (23) the fact that the sutures can enter the lumen without danger of thrombosis as shown by Dörfler and others, greatly facilitates arterial suture. He advises the use of silk instead of catgut. The silk sutures are quickly covered with fibrin over which the endothelium soon grows.

In 1906 Dorrance[5] reported three cases of complete transverse suture of arteries in animals, in which he used a continuous mattress suture, whipping over the everted edges of the artery after the mattress suture was completed. In two cases the lumen remained unobstructed, in the other complete thrombosis occurred.

The circular suture of veins.—As compared with arteries very few experiments have been made with the circular suture of veins. This is probably due to the fact that the danger of gangrene following the ligation of large veins is, as a rule, less than that following the ligation of the corresponding arteries.

V. Hirsch[6] is said to have successfully sutured the completely divided femoral and jugular veins of dogs in 1881. Murphy in 1897 united the divided jugular vein of a sheep by means of a continuous suture of fine silk, the lumen of the vessel being considerably narrowed by the suture. The vein was examined 28 days later and found to be occluded by adhesion at the line of suture, but no thrombus was present.

In an article published in 1901 Clermont (17) gives an historical review of venous suture and reports his experiments with the lateral and circular suture of veins. The latter were limited to two sutures of the divided inferior vena cava: In one case the ends of the vessel were united by a continuous mattress suture of fine silk, which everted the edges of the vessel and approximated intima to intima; the union was completed by suturing the everted edges together with a continuous whip-stitch of the same material. The vessel was examined a month later and its lumen found to be perfectly smooth and unobstructed. In the other case he invaginated the peripheral end a few mm. into the central and fastened them thus with fine silk sutures which were allowed to enter the lumen. When examined a month later the vein was found to be patent, but greatly contracted. From these experiments and those with the lateral suture of veins, Clermont concluded that the first method is the best for suturing veins.

Payr (36) claims to have obtained excellent results in the union of veins by means of his magnesium protheses, which are applied to veins just as to arteries, except that with veins the peripheral is invaginated into the central end. The method is said to be more easily applied to veins than to arteries, for their walls are thinner and therefore more readily stretched. Here again Payr fails to give the number of his experiments or any exact description thereof.

In 1903 Jensen (40) made 17 experiments with the union of completely divided veins, using the simple suture in seven cases and protheses of various kinds in ten. Of the seven simple sutures four remained patent; of the ten cases in which protheses were used, eight became completely thrombosed and two remained patent. In six of the sutures the following method was used: After inserting two or three tension sutures, a continuous suture including the entire thickness of the vessel wall was applied. In the other case mattress sutures were used. In only two cases was catgut employed and in both thrombosis occurred. Of the ten cases in which protheses were employed, the cylindrical rings recommended by Payr were used in seven, but in only three of these were the rings made of magnesium, the others being made of bone or decalcified bone.

The circular suture of arteries and veins in man.—Cases of suture of completely divided vessels in man have been reported by Murphy, Djemil Pascha, Krause, Kümmell, Payr, Brougham, and probably others.

In 1897 Murphy (10) reported the following case: On September 19, 1896, a young man received a bullet wound in Scarpa's triangle just below Poupart's ligament. When he was first seen by Murphy on October 4, there was a marked thrill and loud bruit in this region and the pulsation in the popliteal and dorsalis pedis arteries was scarcely perceptible. At the operation on October 7, a penetrating wound was found in the femoral artery, which was almost divided, and also a small wound in the femoral vein. After closing the wound in the vein the artery was resected and united by the invagination method, the central end being invaginated into the distal for about one-third of an inch. On removing the clamps there was no leakage and pulsation immediately reappeared in the artery below the anastomosis. There was no disturbance of the circulation of the leg and the patient made a good recovery.

At the International Medical Congress in Moscow in 1897 Djemil Pascha (52) reported two cases of injury of the axillary artery treated successfully by Murphy's invagination method.

Krause (53) in 1900 reported this case in which he resected both the femoral artery and vein: In operating upon a woman, 55 years of age, for a carcinoma, the femoral vessels were found to be involved to such an extent that it was neces-

[5] Vid. supra.

[6] Cit. by Clermont.

sary to resect a portion of them. With the leg strongly flexed the ends of the vessels were then invaginated and fastened thus with sutures which did not involve the intima. Immediately after the operation pulsation could be felt in the artery distal to the suture; the leg had to be amputated later on account of gangrene.

In 1900 Kümmell (54) reported two cases, in one of which he anastomosed the femoral artery, in the other the femoral vein. In removing a carcinoma of the glands of the groin the femoral artery was found to be involved to such an extent that it was necessary to resect 5 cm. of this vessel. This was done in the following manner: After freeing the vessel above and below and applying clamps armed with rubber, the diseased portion was removed and, with the leg flexed at the hip, the central end of the vessel was invaginated ½ cm. into the distal and sutured with fine silk which did not include the intima. This suture was reinforced by a second layer of sutures which included only the adventitia. After a short time distinct pulsation could be felt in the popliteal artery. The carcinoma recurred in a few weeks and death followed in four months; at the autopsy, unfortunately, nothing could be seen of the suture, for the vessel was completely destroyed by the growth.

In the second case it was necessary to resect 2 cm. of the femoral vein, likewise on account of involvement in malignant growth. The ends of the vein were united by means of a continuous suture of fine silk which doubtless penetrated the intima. After removing the clamps the circulation in the leg was reestablished, and the patient made a good recovery.

In 1901 Payr (55) had an opportunity to try his method in man: In extirpating carcinomatous glands of the groin 4.5 cm. of the femoral vein was removed on account of involvement in the growth. The ends of the vessel were united by invagination over a magnesium prothesis after his method. The patient died three days later of pneumonia and examination showed that the lumen of the vein was fully preserved.

In 1906 Brougham (56) reported the following case: A man, 39 years of age, received a stab wound which almost completely divided the axillary artery and vein. The vein was ligated, but the division of the artery was completed, and the ends united by invagination after Murphy's method. The patient made an uneventful recovery.

Remarks.—What has been said above, in discussing the external suture of vessels, regarding suture materials, the means of provisional hæmostasis, the question as to whether the suture should or should not penetrate the intima, the need of a perfect aseptic technic, etc., applies equally well to the circular suture.

The methods recommended for uniting completely severed vessels may in general be divided in two classes: (a) Those in which the simple suture is used; (b) those in which mechanical aids are employed.

The suture has been applied in various forms; some have used simple interrupted sutures and mattress sutures, others the continuous suture: some include all the coats of the vessel in the suture, others try to avoid the intima, which in veins is almost an impossibility. Murphy recommends uniting completely divided vessels by invaginating one end a short distance into the other and fixing them thus with sutures.

The mechanical aids may be divided into the extra-vasal and endo-vasal. Among the former may be mentioned various clamps, decalcified bone and ivory rings, sheaths made of sections of other arteries or veins, aluminum rings, magnesium rings, etc. The most important of these are the magnesium rings or protheses of Payr, by means of which the ends of the vessel are so invaginated that intima is approximated to intima. Among the endo-vasal aids we may mention the glass cylinders of Abbe and Gluck, the caramel cylinders of Carrel and the glass bobbins of De Gaetanō. These are of no importance clinically, but are of historical interest.

Although the results of the application of the invagination methods of Murphy and Payr to vessels in man have proven very gratifying, I cannot but feel in the light of the animal experiments of Carrel, Jensen, myself, and others, that the simple suture is preferable to these more complicated procedures. The results obtained in animals by Carrel and myself have been, barring the cases in which infection occurred, almost ideal and seem to demonstrate conclusively that the sutures can penetrate the intima with impunity. The method is simple, easy, and requires no mechanical aid. It seems to me that, just as in intestinal suture we approximate endothelium to endothelium, so in blood vessel suture it is advisable to approximate intima to intima. With Carrel's method traction upon the three primary sutures, during the application of the continuous suture, approximates intima to intima more or less accurately, but the apposition might be improved by substituting U-shaped sutures for the single traction sutures and then applying the continuous suture to the everted edges, as has been suggested by Jensen. The advantages obtained by this method might, however, except with large vessels, be counterbalanced by the constriction produced.

Arterio-Venous Anastomoses.

Circular or end-to-end arterio-venous anastomosis.—The first successful arterio-venous anastomsis was performed by Gluck (35) who united the carotid artery of a dog to the jugular vein by circular suture without thrombus formation. In 1902 Berard and Carrel divided the femoral artery in Scarpa's triangle and sutured the central end of the artery to the peripheral end of the saphenous vein. The anastomosis withstood the arterial pressure and the vein became distended and pulsated actively, but no physiological results were observed, as the animal died of infection two days after the operation. In the same year these experiments were continued by Carrel and Morel (57), who succeeded in anastomosing the central end of the carotid artery into the peripheral end of the external jugular vein without subsequent thrombus formation. Several weeks after the operation, when the animal was presented before the "Société nationale de médecine," the external jugular vein pulsated actively and a loud systolic murmur could be heard at the point of anastomosis. During

the several months the animal was under observation the results remained satisfactory.

In 1902 San Martin y Satrustegui (58) also experimented with the circular arterio-venous anastomosis. He made a series of 40 experiments on dogs, operating by preference in the groin, but also in the neck and other regions traversed by large blood vessels. The femoral vessels were separated and the central portion of the femoral vein ligated. Forceps were then applied to the central portion of the artery and the distal portion of the vein and the vessels divided; there was no bleeding from the distal end of the artery, although it was not clamped or otherwise occluded. The central end of the artery was then united to the distal end of the vein by invaginating the artery into the vein and suturing them with catgut. On removing the clamps the arterial blood flowed into the vein and the distal portion of the artery, which had remained bloodless during the operation, in 30 to 60 seconds after the current was turned on, began to carry fluid which looked like a mixture of arterial and venous blood, as though the current had been reversed. This end of the artery was then ligated, the wound closed, and the animal allowed to live. In later cases St. Martin saw the saphenous vein fill and change color as soon as the arterial blood was turned into the femoral vein.

All of the animals stood the operation well, except those whose peritoneum was invaded. One of the more vigorous dogs lived eight days with anastomosis of the carotid artery and jugular vein on both sides, death being due to hæmorrhage, or asphyxiation from enormous œdema of the neck. Few of the dogs had œdema, but in many there was a hæmorrage on the eighth day, which was often fatal. As to the cutaneous wound, it healed usually by first intention, sometimes there was a little suppuration, and in two or three cases a real phlegmon. The specimens were examined at periods varying from 48 hours to 20 days after the operation. The vessels were found completely obliterated by extensive thrombi, which, in the late examinations, were already organized. In one case the vessel remained pervious for two days, but in some instances coagulation took place even before the current was turned on.

In 1903 Exner (59) undertook certain experiments with the intention of studying the changes which veins undergo under arterial blood pressure. In four dogs he united the central end of the carotid artery to the peripheral end of the external jugular vein by means of the magnesium protheses of Payr. The wounds healed without reaction, but when examined two to six weeks after the operation, the vessels were found to be completely thrombosed. Höpfner (30) in 1903 also experimented with arterio-venous anastomoses, using the protheses of Payr. In all of his cases there was thrombus formation which he attributed to degeneration of the thin vein wall, produced by the high arterial tension.

In 1905 the experiments begun in France by Carrel and Morel were continued in this country by Carrel and Guthrie (60), (61), (62), (63), and, with improved technic, various arterio-venous anastomoses were done with very successful and interesting results. The technic is thus described by Carrel: "The threads and needles were the finest and strongest obtainable. The threads were sterilized in vaseline and applied when heavily coated with the same. The vessels were handled very gently and the endothelium was protected from drying by isotonic sodium chloride solution or by sterilized vaseline. No dangerous metallic forceps were used. The greatest care was exercised to obtain accurate and smooth approximation of the endothelium of the vessels. Finally, we developed a technic which is equally well adapted for arterio-arterial, veno-venous or arterio-venous anastomoses, and which yields uniformly successful results."

Circular or end-to-end arterio-venous anastomoses may be divided in two classes; viz., (a) uniterminal, and (b) biterminal arterio-venous anastomoses. The former will be discussed now, but the latter will be considered when we describe the implantation and transplantation of arteries and veins.

Concerning uniterminal anastomoses Carrel and Guthrie write as follows: "The termino-terminal anastomosis may be performed in nearly all cases even when the size of the vessels differs greatly. An artery may be easily united to a vein of twice its caliber. On the contrary, it is more difficult to unite a small vein to a large artery, for the venous wall is easily folded, while the artery on account of its thick walls is not. The more nearly similar the diameter of the vessels, the more easily successful anastomosis may be performed. When the vein is much larger than the artery and the consequent foldings of the vein in making the anastomosis are irregular, as may happen if the operation is performed without sufficient care, hæmorrhage occurs at the line of union. Fibrin may be deposited in the bottom of the foldings and in the miniature gaps occurring between the endothelial coats of the artery and vein. Therefore, when the difference in size of the artery and vein is too great, instead of end-to-end anastomosis, it is better to perform lateral implantation of the end of the vein into the wall of the artery.

"This termino-lateral arterio-venous anastomosis is more difficult than the former. It should be used only when the end-to-end anastomosis seems inadvisable, owing to the difference in size of the vessels or when the experimental result sought for indicates it. For instance, when a segment of intestine is transplanted into the neck for the purpose of establishing communication between the cut ends of the œsophagus, the end-to-end anastomosis of the intestinal vein to the jugular vein is impracticable, owing to the enormous difference in the size of the vessels. It then becomes necessary to make a lateral implantation of the end of the small vessel on the wall of the jugular vein. Or this lateral implantation is performed in order to obtain certain modifications of circulation, as, for example, lateral implantation of the central end of the external jugular vein on the common carotid artery, in order to diminish the amount of blood in the peripheral portion of the artery.

"Although the termino-lateral anastomosis is somewhat

more difficult than the end-to-end anastomosis, it is by no means impracticable on this account. By making a triangular opening larger than the lumen of the vein, through the wall of the artery, and taking care to have an accurate approximation of the endothelial surfaces of the vessels, the anastomosis is very satisfactory, as absolutely no blood escapes and no stenosis of the vein is produced.

"A third kind of anastomosis, more rarely used than the kinds above described, may also be mentioned. When the vein is exceedingly small, so small that a direct anastomosis is impossible, it is dissected as far as its junction with a larger vein. The wall of this vein around the mouth of the small vessel is then resected and grafted onto the wall of the artery.

"As previously stated this paper will deal mainly with the transplantation of veins onto arteries.

"There are six possible varieties of this operation, as the central end or the peripheral end of the vein may be united to the central end, the peripheral end or the wall of the artery. But as the anastomosis of the central end of the artery to the central end of the vein is practically the same in result as lateral implantation of the artery onto a vein, and as anastomosis of the peripheral end of the vein to the wall of the artery produces practically the same results as the anastomosis of the peripheral end of the vein to the central end of the artery, they do not deserve special mention. Four varieties only will therefore be described.

"1. *Union of the central end of the vein to the peripheral end of the artery.*—Anastomosis of the central end of the external jugular vein to the peripheral end of the common carotid artery is an example of this kind of operation. It produces a vessel composed in its upper portion of the carotid artery and in its lower portion of the external jugular vein. The pressure in this portion of the artery becomes lower than the normal blood pressure and the direction of the blood stream is reversed. The jugular carries toward the heart red, instead of dark blood. As a result, functionally, the carotid artery becomes a vein filled with red blood, being comparable in this respect to the pulmonary vein. It is probable that the wall of the artery undergoes marked anatomical changes. Owing to the lowering of the blood pressure, its wall may become thinner and the elastic and muscular layers modified, but at the present time we cannot go further into the point. But, as we have a dog in good health upon which this operation was performed nearly seven months ago, we shall subsequently be enabled to discuss it further.

"2. *Union of the central end of the vein to the wall of the artery.*—It is evident that after this operation a large part of the red blood of the artery returns toward the heart through the veins. In several cases the central end of the external jugular vein was united to the wall of the carotid artery. An abundant portion of the red blood flowed into the vein through the anastomosis with a strong thrill. The vein retained its venous functions, i. e., it conveyed blood toward the heart, but was filled with arterial blood. The artery also retained its normal functions, but its blood pressure was lowered. Tracings were taken, and they showed that after the establishment of the circulation through the anastomosis, the blood pressure in the artery is markedly diminished. This result is quite natural, for the lateral implantation of the central end of the jugular onto the wall of the carotid artery permits of a kind of continuous hæmorrhage from the carotid into the vein. When this operation is made on the jugular and the carotid it does not apparently alter the character of the circulation in general.

"3. *Union of the peripheral end of the vein to the peripheral end of the artery.*—This operation was performed on arteries having no, or very small collaterals. The result was the reversal of the circulation through the vein. The artery becomes filled with dark blood, venous in character. If, for instance, the peripheral end of the right renal vein be united to the peripheral end of the left renal artery, the dark blood from the right renal vein would flow through the left renal artery, the left kidney, the left renal vein and thus into the vena cava.

"4. *Union of the peripheral end of a vein to the central end of an artery.*—It is evident that, from a functional point of view, the operation transforms the vein into an artery. Several series of experiments were performed. The external or internal jugular or the thyroid veins were united to the carotid artery; the femoral or long saphenous veins to the femoral artery; and the inferior vena cava to the aorta.

"*The transplantation of the peripheral end of the external jugular vein onto the central end of the common carotid artery.*—The right external jugular vein was exposed, thoroughly dissected and cut near the root of the neck. Its peripheral end was inserted between the sterno mastoideus and the sterno hyoideus muscles and united behind the trachea to the central end of the left carotid artery. On release of the hæmostatic clamps, the vein became filled with red blood and pulsated like an artery, it being transformed from a functional standpoint into an external carotid artery. The vein is able immediately to perform the more important arterial functions. Its wall adequately supports the increased blood pressure. Even when the carotid artery is anastomosed to a more delicate vein, such as the internal jugular or thyroid, the sudden increasing of the pressure apparently does not injure the wall. In size the vein always appears to be very much enlarged. Clinically, this operation does not produce general or local symptoms if it deals only with vessels like the carotid and the external jugular vein. Even when the central end of the carotid is anastomosed to the peripheral end of the internal jugular vein the dog manifests no abnormal symptoms. A dog on which the operation was performed three months ago is now living and appears absolutely normal in all respects.

"In some cases the anastomosis may produce very dangerous effects. If, for instance, the central end of the abdominal aorta is united to the peripheral end of the vena cava, the circulation is immediately reversed in the lower part of the abdomen and the upper part of the inferior limbs, the valves stopping the blood from the lower portion of the latter for a

time. By degrees, however, they give way, and at the same time the animal may present symptoms of a very abundant hæmorrhage even becoming comatose. If at this stage the head be lowered and the posterior limbs elevated, it immediately regains consciousness, as evidenced by its cries and the ambulatory movements of the forelimbs. Post-mortem examination of such a case shows an enormous congestion of the veins below the level of the anastomosis, the animal dying apparently by hæmorrhage of the red blood into the venous system.

"After the operation the veins undergo a rapid structural modification, seemingly of an adaptive character, in order to meet the imposed arterial functions. The wall becomes thickened, owing, probably, to the increase of blood pressure, for if the vein has numerous collaterals, and consequently a relatively low blood pressure, the thickening is less rapid and marked. In a case of anastomosis of the central end of the carotid to the peripheral end of the jugular the specimen was taken five weeks after the operation. From the anastomosis to the first collaterals the wall was thicker than the wall of the carotid artery. Between the first and second collaterals the thickening was less marked. In the superior part of the neck, above numerous collaterals, the thickening was hardly apparent. When the vein has no collaterals, or when the collaterals are ligated, the transformation of the wall is very rapid and marked. After a few weeks the thyroid vein becomes very similar in size to the thyroid artery."

Carrel and Guthrie (64) claim to have produced an actual arteriosclerosis of an artery by suturing it into a relatively small vein. The macroscopic modifications of the artery are characterized by a slight retraction of its lumen and by a marked increase in the thickness and rigidity of its walls. The histological changes consist of an hypertrophy of the middle coat, which is due to an increase in the number and size of the muscle and elastic fibers and an hyperplasia of the interstitial connective tissue. The sclerosis of the adventitia may be regular or irregular. The same is true of the intimal sclerosis, which may present itself in the form of a regular thickening of the intima or may be much more marked in certain places than in others. The regions of greatest thickening of the intima and adventitia correspond to the places where the media is thinner. It seems that the arterial wall reacts first by an hypertrophy of the muscle layer and that the sclerosis of the intima and adventitia comes later. In a case observed three months and ten days after the operation the hypertrophy of the muscle was strongly marked, whereas, the intimal sclerosis was slight. In another case observed six months after operation the muscular hypertrophy was somewhat greater than in the preceding case, while the intimal sclerosis was much greater. No atheromatous lesions were observed.

When arterial tension is lowered by anastomosing an artery into a large vein the wall of the artery becomes thinner and its lumen larger. The muscular and elastic constituents of the medial coat diminish in number and volume.

Lateral arterio-venous anastomosis.—After his experiments with end-to-end arterio-venous anastomoses had failed, and arguing that arterio-venous aneurysms are well borne in man, San Martin y Satrustegui (58) in 1902 began to experiment with the lateral anastomosis of arteries and veins in goats. After opening the carotid artery and internal jugular vein in the neck, temporary hæmostasis was produced by small rubber tubing placed about the vessels at either end of the wound and openings 1 cm. long made in the vessels. The edges of the openings were then united by means of continuous sutures of fine silk, the posterior row of sutures apparently being placed from within the lumen. Two animals were thus operated upon and the result was said to be the same in both cases, though only one section was described. In this case which was examined three months after the operation, the carotid pulsated strongly and retained its original dimensions; the vein, however, was atrophied and almost empty of blood proximal to the anastomosis, but peripheral to the anastomosis was distended with dark blood and did not pulsate. The site of the anastomosis could hardly be determined by simple inspection, but seemed to correspond to the point where the vein suddenly became contracted. No opening could be demonstrated by injecting water into the vessels. From microscopic examination, however, St. Martin concluded that a small opening persisted.

Arterio-venous anastomoses in man.—From these experiments, although they could scarcely be called successful, St. Martin concluded that such an operation might be of value in treating gangrene due to arterial sclerosis. He tried it clinically in two cases. The first case was a man, 52 years of age, with gangrene of the toes extending onto the metatarsus. No pulsation could be felt in the dorsalis pedis, posterior tibial or even in the popliteal artery. The femoral pulsated strongly in Scarpa's triangle. An incision was made in Scarpa's triangle and the artery easily isolated, but the vein was freed with difficulty, being rather adherent. Temporary hæmostasis was produced by rubber tubes held with clamps. Openings 8 mm. long were then made in the vessels and a fairly satisfactory anastomosis obtained. After removing the ligatures the arterial blood passed through the artery to the limb, but the vein did not change color, either because the anastomotic opening was too small or because the walls of the vein had lost the little elasticity which they normally possess. The wound was closed and the gangrenous portion of the foot removed. The immediate result of the operation was fairly satisfactory; the pains became less, either because the gangrenous portion was removed, because the nerves had been separated from the vessel sheath to which they were quite adherent, or because, thanks to the anastomosis, the leg was better nourished. Unfortunately, this condition did not continue long and symptoms appeared which required amputation of the leg through the calf. The arteries were greatly sclerosed; the vein, however, appeared normal with the exception of some atrophy, probably from disuse. St. Martin thought the veins might have assumed the function of arteries if the operation had been done earlier and been more successful. Sometime later amputation through the middle of the

thigh resulted in death. The specimen showing the anastomosis was not examined, at least it is not described.

The other case was a man, 66 years old, who had gangrene of the toes. The same procedure was adopted as in the foregoing case. The artery and vein were so adherent to each other that, for hæmostasis, it was necessary to place the rubber bands about the two together. The nerve, however, was carefully separated. Very small openings were made in the artery and vein, which were united by continuous sutures. After removing the ligatures the vessels filled out, but the walls of the vein were so thick that one could not see whether arterial blood passed into the vein through the small wound. The wound in the groin was closed and the foot amputated. The patient made an uneventful recovery, but nothing is said of the subsequent behavior of the vessels.

In 1902 Jaboulay (67) reported the following case: A man, aged 47, had senile gangrene of the right foot which required amputation, first of the foot and then of the thigh. Sometime later gangrene began in his left foot and Jaboulay performed a lateral anastomosis of the femoral vessels in Scarpa's triangle. Thrombosis, which was attributed to the presence of an arterio-sclerotic placque, occurred at the site of suture, and it became necessary to amputate through the thigh.

In 1903 Gallois and Pinatelle (68), assistants of Jaboulay, reported this case and published the results of certain experiments, which they had made, to investigate the possibility of a reversal of the circulation in the head, arms, and legs. In order that such a reversal of circulation may take place they pointed out that the following obstacles must be overcome: (a) The valves; (b) the numerous venous anastomoses, which create short circuits and lower the blood pressure; (c) the resistance of the capillaries. Their experiments were done on the cadaver. A colored fluid was injected under pressure into the main vein of the member, but immediately returned by the other veins. After these were occluded it was impossible to force the fluid into the main vein, although considerable pressure was used. They concluded that, experimentally the circulation through the main vein of a limb, in a direction opposite to that of the normal current is prevented by the valves. They realized the fact, however, that, clinically, the valves can be forced and the current reversed in the veins, for they had observed cases of arterio-venous aneurysm, in which the veins of the limb, even at considerable distances from the aneurysm, were markedly dilated and pulsated actively.

Carrel and Guthrie (69) (70), who attribute the failure of the experiments of Gallois and Pinatelle to the fact that they operated upon the cadaver and not upon living tissues, which have a great adoptive power, seem to have proven that a reversal of the circulation in a limb of a dog is possible by establishing an end-to-end arterio-venous anastomosis. An experiment on a dog showed that three hours after a *termino-terminal* anastomosis of the central end of the femoral artery to the peripheral end of the femoral vein, the veins of the thigh, the leg, and the foot were filled with red blood, and that the dark blood returned to the heart through the arteries. They found that: (a) The valves prevent, at first, the reversal of the circulation in the veins; (b) after a short time the valves gradually give way and the red blood flows through the veins as far as the capillaries; (c) finally, it passes through the capillaries and the arteries are filled with dark blood. Probably the dark blood also returns from the capillaries toward the heart through some of the veins; (d) practically complete reversal of the circulation is established about three hours after the operation. However, when a *lateral* arterio-venous anastomosis has been done, the larger part of the arterial blood, instead of going toward the capillaries, returns to the heart through the central end of the vein and at the same time the arterial blood pressure is lowered. Experiments have shown that: (a) After a lateral arterio-venous anastomosis a very large portion of the red blood returns immediately toward the heart through the central end of the vein; (b) the peripheral portion of the vein and its branches are distended and pulsate, but the valves are not forced and the red blood does not circulate through them; (c) three hours after the operation all the valves are yet competent and no beginning of a reversal of the circulation can be detected.

If this be true very little can be expected from the treatment of senile gangrene by lateral arterio-venous anastomosis.

In 1906 Hubbard (71) reported the following case, in which he performed a crossed arterio-venous anastomosis of the femoral vessels for senile gangrene of the toes. The patient, a man 80 years old, was admitted to the hospital with dry gangrene of the middle toe of the right foot. There was a general arteriosclerosis and no pulsation could be felt in the dorsalis pedis of this foot. In spite of appropriate treatment the gangrene extended and involved the neighboring toes. Operation: The femoral vessels were exposed at the apex of Scarpa's triangle and a crossed arterio-venous anastomosis performed by invaginating the central end of the artery into the peripheral end of the vein and the peripheral end of the artery into the central end of the vein, and suturing them thus with fine Pagenstecher's thread. After the first anastomosis had been completed, and the means of provisional hæmostasis removed, the vein partially filled and pulsated slightly. During the manipulations the controlling tourniquet was pulled off the peripheral end of the artery and a considerable amount of dark, venous-looking blood escaped. It is hardly possible, however, that the circulation could have been reversed in such a short time. The cutaneous wound was closed with silk-worm gut and a plaster cast applied with the thigh flexed on the body to relieve tension on the vessels.

The patient made a good recovery, but the gangrene subsequently extended to the tarso-metatarsal joint, where a line of demarcation formed. At this time the author thought he was justified in making the following deductions: "Inasmuch as the circulation in the leg before operation was sufficiently poor to permit gangrene of the toes, and inasmuch as the femoral artery had been divided in Scarpa's triangle thus permitting collateral circulation only through the profunda, it was

fair to suppose that very little blood would have reached the lower leg through the collateral circulation, and that the gangrene would have rapidly involved the leg unless as a result of the operation the veins were carrying arterial blood." The lower portion of the leg and foot were amputated some time later. At this operation, which was performed without a tourniquet, the anterior and posterior tibial arteries were found to contain arterial blood, which spurted from the cut ends with fairly good force, and the veins did not appear to contain any arterial blood. These findings probably vitiate the previous deductions.

The application of arterio-venous anastomoses to the direct transfusion of blood.—Arterio-venous anastomoses have been employed by Crile and Dolley in the direct transfusion of blood in animals. From a large series of experiments they have drawn the following conclusions:

"Arteries and veins of varying sizes may be readily anastomosed by Carrel's method so as to be impervious to blood and free from clotting; the transference of blood from one animal to another is most definitely accomplished by anastomosing the proximal end of an artery of the donor into the proximal end of the vein of the donee: convenience may be the only consideration in the selection of the vessels to be anastomosed; the blood of one animal may be rapidly transfused to another; the blood of one dog is isotonic with that of another dog; if a dog be bled to the last drop of blood that will flow, and then an equal amount of blood be transfused from another, the transfused blood suffers no impairment by the blood or tissue of its new host, and, in turn, it causes no impairment; no hæmolysis is produced; and, finally, the transfused blood becomes a perfect substitute for the lost blood, and the factor of hæmorrhage may be eliminated."

Crile (72), who has applied the same method to various clinical cases, has obtained some brilliant results, especially with cases of hæmorrhage.

The author has transfused blood by this method in four cases, two of these being extensive burns, one a case of post-operative hæmorrhage in a jaundiced patient, and the fourth a case of pernicious anæmia. The results in these cases, which have not been studied as carefully as they should have been, were somewhat disappointing. I will now describe them in some detail.

CASE I.—The patient, a woman, 41 years of age, was admitted on February 5, 1907, with history and physical signs pointing to stones in the common duct. The jaundice, which had been present with varying intensity for ten weeks, became quite intense two weeks before she came to the hospital and remained so up to the time of her admission. Her coagulation time was considerably delayed, being 12½ minutes. At the operation on February 8, 1907, numerous small stones were found in the gall bladder and several large stones in the common duct, which could be removed through the greatly dilated cystic duct. A portion of the gall bladder was excised, the mucosa of the remaining portion being curetted and swabbed with pure carbolic acid. A tube was sutured into the cystic duct and an iodoform gauze pack placed down in the remains of the gall bladder. One bleeding point on the lesser omentum was ligated; otherwise the abdomen seemed perfectly dry.

A few hours after the operation the patient began to show signs of hæmorrhage which in six hours became quite alarming. The patient was pale, perspiring profusely and the pulse was 140 to the minute, and very weak. The dressings were saturated with blood and when these were removed a considerable ooze could be seen around the gauze drain. The wound was packed tightly with gauze, a tight binder applied to the abdomen, the legs bandaged and subcutaneous infusions of saline solution and other stimulants administered. In spite of this treatment the patient's condition steadily became worse until ten hours after the operation it was so critical that it was decided to do a direct transfusion of blood. At this time the patient was extremely pale, quite drowsy and the pulse could just be felt at the wrist, but could not be counted accurately. A man in one of the public wards kindly volunteered to donate the blood. Under cocaine anæthesia the left radial artery of the donor and the median basilic vein of the donee were exposed and, after applying small spring clamps armed with rubber, were divided. The proximal end of the artery of the donor was then sutured to the proximal end of the vein of the donee by Carrel's method. The suture was fairly satisfactory, there being no bleeding when the clamps were removed. The small size of the radial artery was, however, rather disappointing and during the operation the exposed portion of the vessel seemed to steadily contract in spite of the application of warm normal saline solution. The transfusion was continued for about 110 minutes. At the end of this time the vein was divided and the blood allowed to run into a receptacle for a few minutes. This blood was measured and, allowing for the time the stream had been turned on, it was estimated that the donee had received between seven and eight hundred cc. of blood. During the transfusion the condition of the donee improved somewhat but not so much as I had hoped and expected. After the operation she seemed brighter, said she felt better, her color was distinctly better and her pulse stronger but still quite rapid—140 to the minute. Hæmoglobin and blood pressure estimations were, unfortunately, not made. The donor showed the effects of the loss of blood very little, the blood pressure falling from 140 to 115.

The improved condition of the donee lasted only a short while. The hæmorrhage continued and she died five hours after the transfusion was completed. The abdominal wound was opened and the abdominal cavity found to contain 500+ cc. of blood.

Transfusions in the next two cases were undertaken, at the suggestion of Dr. Halsted, hoping that the blood pressure of the donees would be so increased by the transfusion that they could be bled from the opposite arm and the toxæmia, produced by the burn, thus combated.

CASE II.—The child, 3½ years old, was admitted on February 20, 1907, with an extensive superficial burn, involving the right half of the trunk, right arm, right side of the face, and, to a slight extent, the left arm and right leg. After being admitted to the hospital the condition of the patient became rapidly worse and in 48 hours it was critical; the pulse which on admission was 128 to the minute, was then 180, but of fair quality; the temperature, which on admission was 99°, had risen to 105°. The child was quite dull and hard to rouse. The following day the temperature was 103.8° and the pulse 170 to the minute, but its quality was poorer than on the previous day and the stupor was more pronounced, it being very difficult to rouse the child to take nourishment. In view of the toxic condition, high temperature, and rapid pulse it was decided to do a direct transfusion of blood, a relative of the patient consenting to give the blood. The operation was done practically as in the foregoing case,

except that, on account of the small size of the donee, the brachial vein was used instead of the basilica. The suture was quite satisfactory considering the small size of the vessels. On turning on the blood stream the vein became considerably distended and pulsated actively and it seemed as though the child was receiving a considerable amount of blood. Blood pressure observations, however, on the child showed no increase in pressure during the 30-40 minutes, during which the transfusion continued. After this time pulsation in the vein ceased and it was thought that thrombosis had occurred; accordingly, the vessels were ligated and that portion containing the suture was removed for examination. This examination revealed a small thrombus, adherent to the line of suture, which had probably occluded the vessel. The donor was little, if at all, affected by the bleeding. As said above, there was no increase in the blood pressure of the donee, so it was not considered wise to bleed from the opposite arm. Although it may be a case of *post hoc ergo propter hoc*, the child improved rapidly after the transfusion and is now (March 20, 1907), apparently on the road to recovery, though the temperature continues somewhat elevated.

Case III.—This patient, 4 years old, was admitted to the hospital with an extensive burn, involving the greater portion of the trunk, the face, the thighs, and parts of the arms. Her condition was critical and, in spite of appropriate treatment, steadily became worse, until, twelve hours after her admission, it was such that it was decided to do a transfusion of blood, intending, if possible, to raise the blood pressure to such an extent that the child might be bled from the opposite arm. At this time the child was pale, its extremities were cold and clammy, it was vomiting frequently and its pulse could hardly be felt. A man in one of the public wards kindly consented to give the blood and the operation was done exactly as in the preceding case. The anastomosis was very satisfactory. On removing the clamps the vein became distended and pulsated actively, and when pressure was made upon the vein it became so distended in the region of one of its valves that it looked as though it would burst. The transfusion was continued for 83 minutes, when the vein was divided and the blood found to be running at the rate of 4 cc. to the minute. It was thus estimated that the donee had received 332 cc. of blood. That portion of the vessels containing the suture was removed. On being opened it was found to be perfectly smooth and no thrombus was present. The condition of the child improved somewhat during the transfusion, its color improved and the quality of the pulse became such that it could be counted. The improvement was, however, disappointing and far from enough to warrant bleeding from the opposite arm. The donor showed the effects of the bleeding very little, his blood pressure falling from 120 to 105. The improvement of the child was of short duration, and it died about six hours after the transfusion was completed.

Case IV.—The fourth was an advanced case of pernicious anæmia, who had only 848,000 red blood cells to the cubic millimetre and whose hæmoglobin was reduced to 22 per cent. The transfusion was done largely in order to study the changes in the blood picture and to see how long the improved condition would last. The donor was a man with polycythæmia, whose red blood count was 8,712,000 and whose hæmoglobin was 123 per cent. In this case in order to avoid the contraction of the radial artery, if possible, it was not dissected out cleanly, as in the previous cases, but its venæ comites were left attached to it, except at the point where it was divided. In spite of this precaution, however, a good deal of contraction did occur. The artery of the donor was sutured to the proximal end of the median basilic vein of the donee as in the other cases. The suture was very satisfactory; no hæmorrhage occurred when the clamp was removed from the artery, the vein became distended and pulsated actively. After eighty minutes the vein was divided and the blood was found to be flowing at the rate of 16 cc. to the minute. It was thus estimated that the donee had received 1280 cc. of blood. At the end of the transfusion there was a perceptible flush to his face, conjunctivæ and finger nails, but there was no marked change in his subjective sensations. A blood count, made at this time, showed that the number of red cells had risen to 1,880,000 and the hæmoglobin to 38 per cent. The donor was not much affected by the bleeding; his blood pressure fell from 150 to 110, his red count to 6,912,000 and his hæmoglobin to 107 per cent.

The improved condition of the donee was of short duration. The daily blood examination showed a rapid diminution in the number of the red cells and amount of hæmoglobin; and in three days they were less than before the transfusion.

While all of these cases seemed to show some improvement as a result of the transfusion, the amount of improvement was disappointing; the cases, however, were very unfavorable ones. A striking feature of all of the experiments was the small size and great contraction of the radial arteries of the donors, which allowed a very slow rate of flow.

Implantation and Transplantation of Arteries and Veins.

In 1896 Briau and Jaboulay (32), experimenting upon animals, after having removed small sections of arteries reimplanted them by circular sutures. The vessels were examined three or four days after the operation, and in all the cases occluding thrombi were present. In an article published in 1898 Gluck (35) mentions having transplanted a portion of the jugular vein into the carotid artery of a dog. The section of vein healed in and there was no secondary hæmorrhage, but thrombosis occurred.

In 1903 Exner (59) experimented with the transplantation of blood vessels using the magnesium protheses of Payr. In six animals he transplanted portions of the external jugular vein into the carotid artery, but in all the cases thrombosis took place. In two dogs pieces of jugular vein, 4 cm. long, were transplanted into the opposite jugular vein, and in two other animals the same was done with the carotid arteries. In these cases also thrombosis was always present when the specimens were examined. Exner thought the failure of the latter experiments was due to the poor nourishment of the transplanted vessel, resulting from disturbance of the vasa vasorum.

In the same year Höpfner (30) performed some experiments with the implantation and transplantation of vessels, and obtained more or less successful results. He likewise employed the magnesium protheses of Payr. Of two cases, in which sections of the carotid were removed and reimplanted, one was successful when examined four weeks after the operation. In one dog a section of the carotid 3 cm. long was transplanted into the femoral artery and a section of the femoral of the same length into the carotid; when examined eight weeks later there was no thrombosis, almost no constriction of the vessels, and their intima was smooth. In another experiment a portion of the carotid of one animal was transplanted into the femoral of another animal, and a

portion of the femoral of the latter into the carotid of the former. The second experiment was successful, and the first was not, probably due to the fact that the wound in the neck healed per primam, whereas the wound in the groin healed by granulation. In 10 experiments, in which sections of veins were transplanted into arteries, although the technic was the same as in the other experiments and care was taken to have the valves of the veins point in the right direction, thrombosis always occurred. Höpfner concluded that such transplantations offer little prospect of being successful, for, when the current is turned on, there is a marked dilatation of the vein, and more or less stagnation of the blood, which leads to thrombus formation. In three experiments sections of vessels were transplanted from one animal species to another, but the result in all cases was negative.

Carrel and Guthrie, who, in this branch of vascular surgery also, have obtained the most remarkable results, speak of an autoplastic transplantation, when the section of vessel is taken from one vessel and transplanted into another vessel of the same animal, a homoplastic transplantation, when the section of vessel is taken from another animal of the same species, and a heteroplastic transplantation when it is taken from an animal of a different species. As a matter of fact, clinically it would be unnecessary to perform any but an autoplastic transplantation, for we can easily extirpate a short section of vein without interfering with the general circulation.[7]

Transplantations may be (a) complete or (b) incomplete. In complete transplantations the segment of vessel is completely excised and then sutured between the cut ends of the other vessel. In incomplete transplantations the middle portion of the segment of vessel is allowed to remain attached to the surrounding tissues and to its branches; for example, a section of femoral vein can easily be isolated without disturbing its connection with the surrounding tissues and sutured between the cut ends of the accompanying femoral artery.

On removing the hæmostatic clamps, after transplanting a segment of vein into an artery, the segment of vein becomes distended with red blood until it is usually considerably larger than the artery, but, although they may be quite thin, its walls adequately support the arterial blood pressure. The pulsation in the vein is less marked than in the artery, for the vein is usually so distended that there is little excursion of the pulse wave. When the transplantation is incomplete and the segment of vein has branches, these branches do not immediately transmit arterial blood. At first they are filled with venous blood, which becomes displaced by the arterial blood as the valves are gradually forced. The branches then virtually become arteries.

[7] Since the preparation of this paper a very interesting article by Stich, Makkas, and Dowman has appeared in the "Beiträge zur klin. Chir.," Bd. 53, 1907, S. 113. Making use of the Carrel method of suture, the authors have obtained excellent results in the circular suture of arteries and the transplantation of arteries and veins. In a number of cases they have succeeded in transplanting sections of arteries from one animal species into another.

After the complete or incomplete transplantation of a segment of vein into an artery the walls of the vein undergo interesting structural changes. These changes have been studied by Carrel and Guthrie (73) who found the following conditions in a dog, examined 14 days after transplantation. The segment appeared as a dilated portion of the carotid artery, its external diameter being about twice as great as that of the artery. The specimen was opened longitudinally and the diameter of the lumen of the venous segment found to be greater than that of the artery, but less than it was at the time of operation. The endothelium was apparently normal, white, and glistening. The lines of union of the vessels were covered with healthy endothelium. After being cut the segment remained open like an artery. The wall appeared almost three times as thick as the wall of the artery and composed of an external and internal part. The two parts were strongly united, but could be separated by careful dissection. The internal part had the appearance of an arterial wall, its tissues on section being very light in color and very dense. The external part of the wall was almost four times as thick as the internal and its tissue was darker and less dense than that of the internal.

Microscopic examination.—Longitudinal sections were stained with hæmatoxylin and eosin, and Unna's stain for elastic fibers. The wall of the vein was greatly thickened. The intima appeared uniform, and its thickness was about like that of the artery. The tunica media of the venous segment appeared to consist of two layers, an inner, composed of muscle cells and longitudinal elastic fibers, and an outer, consisting mainly of coarse longitudinal, white, connective, and elastic fibers. In neither case were these layers as dense as the corresponding layers in the artery. At the anastomosis the muscular layer terminated mainly by sending elastic fibers to intermingle with similar fibers of the muscular coat of the artery, the muscle cells gradually disappearing. The adventitia also seemed to consist of two layers, an outer layer, composed chiefly of loose connective tissue continuous with the corresponding layer of the artery, and an inner layer, continuous with the outer portion of the granular mass lying between the middle and outer coats of the artery.

Replantation and Transplantation of Organs and Limbs.

The replantation of an organ or limb consists in removing it, replacing it, and re-establishing its circulation by vascular anastomoses. The transplantation of an organ or limb consists in its removal and transplantation into another animal or a different portion of the same animal, its circulation being re-established by vascular anastomoses.

In 1902 Ullmann (74) removed a dog's kidney and transplanted it into his neck, the renal artery being united to the carotid artery and the renal vein to the external jugular vein by means of Payr's protheses. The experiment was said to be successful, the kidney secreting normally after the operation. He does not state, however, how long this condition continued.

Three months after this report, Ullmann (75) reported having transplanted the kidney of one dog into another and the kidney of a dog into a goat. He exhibited the latter animal, and demonstrated the functionating kidney. When asked concerning the fate of the dog into whose neck the kidney had been transplanted, he did not say how long the animal had lived or how long the kidney had functioned. He said, however, that the kidney had been removed and on macroscopic examination several necrotic areas were seen; otherwise the kidney seemed normally nourished and had grown to the surrounding tissues.

In 1902 DecAstello (76) also reported experiments with the transplantation of kidneys. He extirpated the kidney of a large dog and transplanted a kidney from another dog into its place uniting the vessels by means of protheses. The animal lived 40 hours during which time 1200 cc. of urine was secreted. Death was due to hæmorrhage resulting from separation of the venous anastomosis.

In 1905 Floresco (77) reported certain experiments with the transplantation of kidneys. After several unsuccessful attempts he succeeded in extirpating the kidney of one dog and transplanting the kidney of another dog into its place the vessels being united by sutures. The end of the ureter was sutured into the skin incision. He does not give the ultimate results of the operation.

In one animal Floresco divided the nerves and ligated the lymphatic vessels of one kidney and extirpated the other kidney; in another animal he divided the nerves and anastomosed the renal vein of one kidney and removed the other kidney; and in a third animal he divided the nerves and anastomosed both the artery and vein of one kidney and removed the opposite kidney. All of the animals remained in good health and Floresco concluded that in the dog the renal vessels can be anastomosed, the nerves sectioned, the lymphatics ligated and the ureter anastomosed without the kidney ceasing to function and the dog lives after the other kidney is removed.

Since 1905 Carrel and Guthrie (63) have made numerous experiments with the replantation and transplantation of organs and have obtained some very interesting results. One of their first experiments along these lines was the extirpation and replantation of the thyroid gland with reversal of its circulation (78). The right thyroid gland of a dog was dissected out and all its vessels ligated except the superior thyroid artery and vein. These vessels were divided, the gland removed and then replaced, the circulation being reversed by suturing the artery to vein and vein to artery. Eleven days after the operation the wound was opened and the gland found to be somewhat enlarged, but its hue and consistency were normal. Twenty-five days after operation the condition seemed practically the same. No histological examination was made, however. By reversing the circulation of goitres in dogs they (79) claim to have produced a diminution in the size of the lobe operated upon and in one dog the goitre not only became smaller, but the general symptoms, referable to a hypothyroidism, largely disappeared. They think these phenomena were due to an augmentation of the circulation resulting from the reversal.

Carrel and Guthrie have used two methods of transplanting organs, *transplantation simple* and *transplantation en masse.*

The *transplantation simple* is the method which has been generally employed, but the objections to this method are that the nerves and their sympathetic ganglia are cut off from the organ and the veins are unduly exposed to injury, so that it is impossible to transplant such organs as the testicle and ovary by this method. To obviate these difficulties they developed the technic of *transplantation en masse,* which consists in extirpating the organ together with its surrounding connective tissues, its nerves and ganglia and its vessels with the corresponding segments of the large vessels from which they originate.

Making use of the simple method of transplantation Carrel and Guthrie have transplanted a heart, a loop of intestine, a kidney, and other organs into the neck. While the immediate result was, in most cases, satisfactory, the ultimate result was usually disappointing. A kidney which was thus transplanted, continued to function for some days (80) as thus described.

The kidney of a small dog was transplanted into the neck, the renal artery being sutured to the carotid artery, the renal vein to the external jugular vein and the ureter to the œsophagus. When examined three days later, the kidney was somewhat larger and its hue was darker than normal, but its consistency seemed normal and the pulsations of the renal artery were strong. The secretion of urine by the transplanted kidney was about five times more rapid than by the normal one. The intravenous injection of normal saline solution caused no change in the rate of secretion in the normal kidney, but markedly increased the rate of secretion in the transplanted organ. The constituents of the urines were similar, but the chlorides appeared more abundant in the urine from the transplanted kidney, while the organic sulphates, pigments, and urea were more abundant in the urine from the normal organ.

The *transplantation en masse* has been used by Carrel and Guthrie (81) (82) in the transplantation of kidneys and ovaries. The technic of these operations is thus described by them.

Both kidneys and the upper portion of the ureters were removed from a small dog, along with their vessels, nerves, nervous ganglia, the surrounding connective tissue, the suprarenal glands, the peritoneum, and the corresponding segments of the aorta and vena cava. The mass was placed in isotonic sodium chloride solution and later transplanted between the cut ends of the abdominal aorta and the inferior vena cava of a bitch. The circulation was reestablished after having been interrupted one hour and a half. Clear urine flowed abundantly from the transplanted ureters which were anastomosed to the normal ones. Both normal kidneys were then removed. The dog recovered rapidly from the operation and remained in good health for eight days, during which time she secreted large quantities of clear urine, which contained no blood and was about normal in composition, the only abnormal constitu-

ent being a small amount of coagulable proteid. The dog died on the tenth day as a result of intestinal obstruction, due to a localized peritonitis on the right side of the abdomen. The circulation of both kidneys was perfect, but there was an enormous hydronephrosis on one side.

Ovaries were transplanted as follows: The specimen, consisting of ovary and a part of the Fallopian tube, united to the segments of the aorta and vena cava by a cellulo-peritoneal ribbon and the ovarian vessels, was taken from one cat and transplanted into another cat from which the corresponding tissues had been removed. The operation is said to have been successful.

Their experiments with *heteroplastic transplantations of organs* were unsuccessful, and they think that, on account of cytolysis, such transplantations are not likely to be successful.

The replantation of amputated limbs.—In 1903 Höpfner (30) experimented with the amputation and replantation of the legs of dogs, uniting the femoral vessels in Scarpa's triangle by means of Payr's protheses. This was done in three animals. In the first case thrombosis occurred on the first day and gangrene followed; in the second case the circulation remained intact 11 days, when death occurred under chloroform, while the dressings were being changed; in the third case thrombosis occurred on the sixth day and gangrene resulted.

Carrel and Guthrie (83) have also made several experiments with the replantation of amputated legs of dogs, but none of these can be said to have been absolutely successful, for, although the circulation remained good for some days, obliteration of the vessels ultimately occurred.

AUTHOR'S EXPERIMENTS.

These experiments were begun with attempts to transplant the thyroid gland, making use of vascular anastomoses by Carrel's method. The attempts proved unsuccessful, so it was decided to apply this method to a series of arterial, venous, and arterio-venous sutures, with a view to determining in what percentage of cases we may expect a successful result.

The experiments were done on dogs of various sizes. When they could be obtained, large animals were used, but often it was necessary to make use of very small ones. The anæsthetic was ether, usually administered after a previous injection of one grain of morphine. The following technic was employed. After shaving a large area, the skin was cleaned with soap and water, permanganate of potash, oxalic acid and bichloride of mercury. The field of operation was then isolated with sterile towels and, after making the skin incision, sterile towels were clamped to the edges of the incision. The vessels were exposed, well freed and provisional hæmostasis produced by small spring clamps whose blades were armed with rubber. The vessels were then divided and prepared for suture by carefully removing the loose connective-tissue sheath about the ends of the vessel. This can be done very nicely by grasping the sheath with forceps, drawing it over the end of the vessel and clipping it off with scissors. The greatest care was exercised in handling the vessels, in order that they be injured as little as possible, and especial care was taken not to apply metallic forceps to the intima. Very fine (No. 16) straight needles and fine China bead silk were the suture materials employed, the thread being greased with or boiled in vaseline as suggested by Carrel. During the operation the drying of the vessels was prevented by the application of normal salt solution or sterile vaseline.

The vessel sutures were done according to Carrel's method. The vessel ends were first united by three interrupted sutures equidistant from each other on the circumference of the vessel, the sutures penetrating all the coats of the vessel. By traction upon these sutures the edges of the vessels were nicely approximated and a continuous suture easily applied. It is convenient to leave the needles attached to the long ends of the primary sutures and to use these ends for the continuous suture. On turning on the current there was seldom any leakage, and when it did occur a slight compression usually caused it to cease in a few minutes. The tissues over the vessel were approximated with fine silk sutures and the skin wound was closed with a subcuticular suture of the same material. The wounds were dressed with silver foil and when the operation was on the neck a crinoline bandage was applied. When the wound was in the groin, it was usually dressed with collodion; sometimes a crinoline bandage was applied, which was usually torn off by the animal within 24 hours. In this connection I should like to thank Dr. R. R. Norris, of Washington, D. C., for his kind assistance in carrying out many of these experiments.

PROTOCOLS OF EXPERIMENTS.

A. CIRCULAR SUTURE OF ARTERIES AND VEINS.

Expers. 4 and 5. Division and suture of both femoral arteries.—March 5, 1906.—Small black hound. The femoral arteries, 4-5 mm. in diameter, were divided and sutured. On removing clamps the left artery spurted at line of suture, two extra sutures being required to check bleeding. One extra suture required on the right side. Sutures only fairly satisfactory, approximation not perfect. No constriction. Active circulation. Subcutaneous tissues sutured with fine silk. Subcuticular skin suture. No dressing.

March 9, 1906.—Left wound seems to be healing well. Skin wound on right leg has broken open. Pulsation well felt in both popliteal arteries.

March 10, 1906.—Dog looks sick. Left wound looks only moderately clean. No pulsation felt in left popliteal artery. Right wound broken open. Pulsation felt in right popliteal artery.

March 13, 1906.—Dog died last night. Autopsy.—Left wound necrotic, though skin edges are still adherent. Hæmorrhage about artery, doubtless due to rupture at suture. Rupture not definitely located. Thrombus adherent to line of suture and occluding the lumen. Right wound broken open, granulating. Thrombus of same nature as on opposite side. Tissues of legs in good condition. No gangrene.

Expers. 7 and 8. Division and suture of the right common carotid and left external jugular.—March 12, 1906.—Small white and yellow shepherd dog. Incision on left side of neck. Left external jugular vein, 6 mm. in diameter, divided and sutured. Carrel's method. Fine white silk, greased with vaseline. Suture satisfactory. No leakage. No constriction of vein. Many su-

tures doubtless pierced intima. Subcutaneous tissues sutured with fine silk. Subcuticular silk suture.

New incision on right side of neck. Carotid artery, 4-5 mm. in diameter, divided. Arterial walls very thick, lumen 2 mm. in diameter. Attempt made to avoid intima. Suture satisfactory. No constriction of artery. Slight leakage. No extra suture required. Carrel's method, fine silk greased with vaseline. Wound closed as on opposite side. Silver foil dressing. Crinoline bandage.

March 21, 1906.—Dog in good condition. Bandage removed. Both wounds healed per primam.

March 31, 1906.—Pulsation felt in carotid distal to suture.

April 9, 1906.—Animal anæsthetized. Vein and artery exposed. Neither at all constricted. Slight ridge on outside of vessels indicating point of suture. Few adhesions about vessels. Pulsation of artery distal to suture as strong as that proximal to suture. Vein fills out when proximal end is compressed. Vessels ligated and portions containing sutures removed for examination. Wounds closed with silk. Crinoline bandage. On opening the artery, after removal, lumen found to be perfectly free, no constriction, intima absolutely smooth. No sutures visible. Lumen of vein also not constricted. Slight roughening of intima at a minute point in line of stuture. No thrombus present. Specimens saved in alcohol (Fig. 1).

Histological examination.—Paraffin sections were stained with hæmatoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. The microscopic study is greatly disturbed by the presence of the sutures which occupy a comparatively large part of the sections. The sutures are surrounded by cellular masses containing numerous small round cells and epitheloid cells, and a few polymorphonuclear leucocytes and giant cells. The intima of the artery is smooth but considerably thickened, the small angle between the everted ends of the inner elastic membrane being filled with new-formed connective tissue derived from the intima. This tissue contains numerous fine elastic fibers. The scar is composed chiefly of connective tissue derived from the intima and adventitia, but the muscle fibers of the media are taking an active part in the restoration of the arterial wall. The elastic fibers of the media and adventitia have as yet invaded the scar very little but next to the scar are very abundant and occur in peculiar whorls. There is a considerable thickening of the adventitia and periadventitial tissues.

The sections of the vein were so distorted by the presence of the sutures that the microscopic examination was of no value.

Expers. 9 and 10. Division and suture of left common carotid and left external jugular.—March 12, 1906.—Small black and white terrier. Left common carotid, 4 mm. in diameter, exposed, divided and sutured by Carrel's method with fine white silk, greased with vaseline. Slight tension. Attempt made to avoid intima, only partially successful. Suture fairly satisfactory. Considerable leakage, controlled by one extra suture. No constriction produced by suture.

The left external jugular vein, 16 mm. in diameter, which was exposed through the same inicision, was divided and sutured in the same way, except that the intima was not avoided. Suture fairly satisfactory. Considerable constriction of vein. Tissues over vessels sutured with fine silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

March 17, 1906.—Dog looks sick, doubtless due to presence of large abscess on side of chest, produced by hypodermic. Abscess opened.

March 21, 1906.—Bandage removed. Slight infection at middle of wound, seems superficial.

April 9, 1906.—Animal lively. Wound entirely healed. Pulsation felt in carotid distal to suture. External jugular fills on pressing vein proximal to suture.

April 23, 1906.—Dog anæsthetized. Vein and artery exposed. No constriction at points of suture. Few adhesions about vessels. Slight ridges on outside of vessels indicating lines of suture. Pulsation in artery distal to suture as strong as that proximal to suture. On being opened both artery and vein were absolutely smooth and free of thrombi. Specimens saved in alcohol (Fig. 2).

Expers. 11 and 12. Division and suture of right common carotid and left external jugular.—March 19, 1906.—Large brown setter. Left external jugular, 7 mm. in diameter, divided near middle of neck, sutured after Carrel's method with fine white silk, greased with vaseline. Some attempt made to avoid intima, not very successful. No leakage. Slight constriction of vein. Another incision on right side of neck. Carotid, 5 mm. in diameter, divided and sutured as above. Attempt to avoid intima, not very successful. Suture fairly satisfactory. No leakage. Tissues sutured over vessels with fine silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

March 28, 1906.—Bandage removed. Wounds healed per primam. Condition of animal excellent.

March 31, 1906.—Pulsation felt in artery distal to anastomosis.

April 23, 1906.—Dog anæsthetized and vessels exposed in region of sutures. Result perfect. Conditions same as in expers. 9 and 10. One or two slight depressions in wall of artery at suture. Vein slightly roughened at one point. Absolutely no constriction of lumen. No thrombosis. Vessels excised and preserved in alcohol (Fig. 3). Wounds closed and animal saved.

Expers. 16 and 17. Division and suture of right common carotid and left external jugular.—April 2, 1906.—Large, curly-haired, black dog. Left external jugular, 7 mm. in diameter, divided and sutured by Carrel's method with fine white silk. Needles and sutures boiled in vaseline. Suture satisfactory. Some leakage which soon ceased without extra sutures. All coats included. Very slight constriction.

Another incision on right side of neck. Carotid, 6 mm. in diameter, divided and sutured as above. Considerable leakage, which soon ceased without extra sutures. All coats of vessel included in suture. No constriction. Tissues over vessels sutured with fine silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

April 12, 1906.—Bandage removed. Wounds healed per primam.

May 5, 1906.—Dog in excellent condition, used in another experiment.

June 23, 1906.—Dog anæsthetized. Vessels exposed. No constriction of either vessel at anastomosis. Very few adhesions about vessels. On being opened intima of both vessels found to be quite smooth. Specimens saved in Kaiserling (Fig. 4).

Histological examination.—Paraffin sections were stained with hæmatoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. The sutures have been almost entirely absorbed and replaced by delicate new-formed connective tissue. The remains of the sutures are surrounded by masses of small round cells, giant cells, and fibroblasts. The intima is smooth and lined by endothelial cells. Here, also, the angle between the everted ends of the inner elastic membrane is filled with connective tissue derived from the intima. No new-formed elastic fibers are seen in this tissue, owing, probably, to the poor staining. There is no regeneration of the inner elastic membrane. The musculature of the media seems entirely restored. The elastic fibers of the media and adventitia are poorly stained and appear to have invaded the scar only to a slight extent. The adventitia and periadventitial tissues are somewhat thickened.

Expers. 20 and 21. Division and suture of left external jugular and right common carotid.—April 23, 1906.—Medium-sized white and black hound. Left external jugular, 7 mm. in diameter, divided and sutured by Carrel's method. Fine white silk boiled in vaseline. All coats of vessel included in suture. No leakage. No constriction.

Right carotid divided and sutured in same manner. Slight

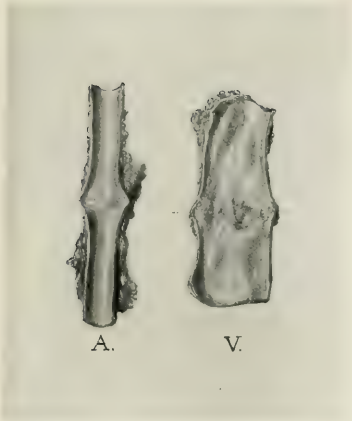

FIG. 1.—Circular suture of carotid artery and jugular vein, 28 days after operation.

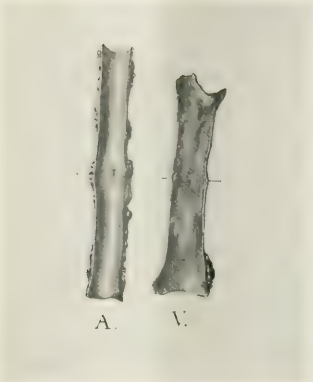

FIG. 2. Circular suture of carotid artery and jugular vein, 42 days after operation.

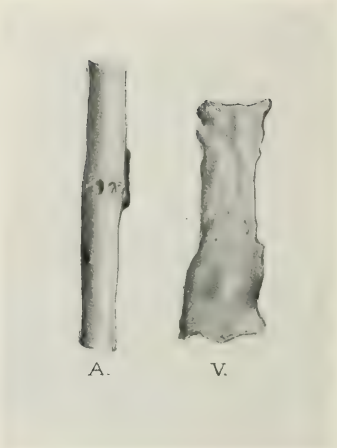

FIG. 3.—Circular suture of carotid artery and jugular vein, 35 days after operation.

FIG. 4. Circular suture of carotid artery and jugular vein, 82 days after operation.

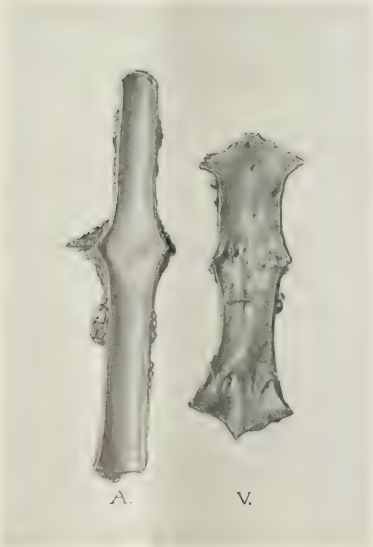

FIG. 5. [illegible] suture of carotid artery and jugular vein, 48 days after operation.

FIG. 7.—Circular suture of carotid artery and jugular vein, 32 days after operation.

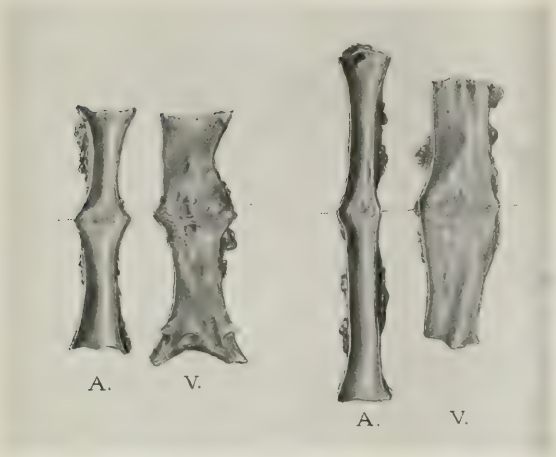

FIG. 6.—Circular suture of both carotid arteries and both jugular veins, 41 days after operation.

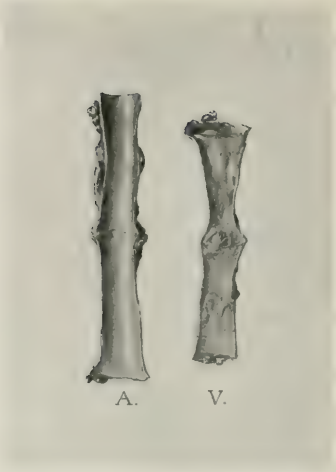

FIG. 8.—Circular suture of carotid artery and jugular vein, 26 days after operation.

FIG. 9.—Circular suture of both carotid arteries, 18 days after operation.

FIG. 10.—Circular suture of both carotid arteries and both jugular veins, 17 days after operation.

FIG. 11.—Circular anastomosis of the left common carotid artery and left external jugular vein, 4 months after operation. As a result of the arterial pressure this vein is much thickened and dilated. Small branch of vein occluded (b), probably due to valves being forced together and becoming adherent.

FIG. 12. Circular anastomosis of carotid artery and jugular vein, 3 months after operation. Marked sclerosis of vein.

FIG. 13. Circular anastomosis of femoral artery and vein, 3 months after operation. Marked thickening and dilatation of vein.

FIG. 14. Circular anastomosis of carotid artery and jugular vein, 40 days after operation. Note thickening and dilatation of vein.

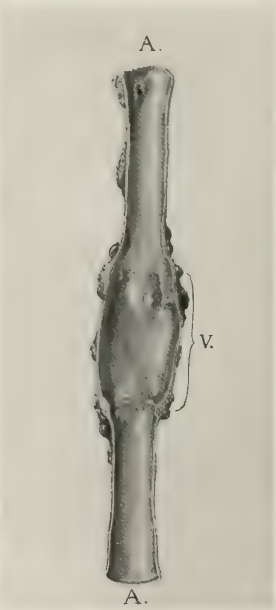

FIG. 15.—Transplantation of section of jugular vein into the carotid artery, 26 days after operation.

leakage, which soon ceased. No extra sutures required. Tissues sutured over vessels with fine silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

May 3, 1906.—Bandage removed. Wounds healed per primam.

June 10, 1906.—Dog anæsthetized. Vessels exposed. Very few adhesions about vessels. Very slight constriction of vein. No constriction of artery. Pulsation in artery distal to suture as strong as that proximal to suture. Vessels opened. Very slight roughening of intima of vein. Intima of artery quite smooth. Specimens saved in Kaiserling (Fig. 5).

Expers. 22, 23, 24, and 25. Division and suture of both external jugulars and both common carotids.—April 30, 1906.—Medium-sized black cur. Both jugulars and carotids exposed, divided and sutured as in previous experiments 20 and 21. Jugulars 7 mm. in diameter. Carotids 5 mm. in diameter. Slight constriction of jugulars at point of suture. No leakage. Left carotid leaked somewhat, requiring one extra suture. Slight leakage from right carotid, which soon ceased. No constriction of arteries, pulsation distal to sutures being as strong as that proximal to sutures. Tissues sutured over vessels with fine silk. Subcutaneous silk sutures. Silver foil dressing. Crinoline bandage.

May 9, 1906.—Bandage removed. Wounds healed per primam.

June 10, 1906.—Dog in excellent condition. Anæsthetized. Both carotids and external jugulars exposed. Few adhesions about vessels near sutures. Pulsation in arteries distal to suture as strong as proximal to suture. Vessels removed and opened. Intima of arteries absolutely smooth. Left vein quite smooth. Intima of right vein slightly roughened by delicate spider-web-like bands, which might have been in process of being absorbed. Right artery and vein in Kaiserling. Left artery and vein in Zenker's fluid (Fig. 6).

Histological examination.—Paraffin sections of the artery were stained with hæmatoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. The sutures are almost entirely absorbed and there are only a few small round cells and giant cells surrounding the remains of the sutures. The intima is smooth and lined by endothelial cells. The angle between the everted ends of the inner elastic membrane, which is not at all regenerated, is filled with a cellular connective tissue, derived from the intima. This tissue contains numerous fine elastic fibers, which toward the lumen are denser, thicker, are very wavy, and apparently take the place of the inner elastic membrane. With the exception of their elastic fibers the media and adventitia are practically restored. The elastic fibers at the edges of the scar are very abundant, form peculiar Medusa-head-like whorls, are evidently involving the scar and would doubtless be entirely regenerated. There is a considerable thickening of the periadventitial tissues.

Expers. 28 and 29. Division and suture of right common carotid and right external jugular.—May 9, 1906.—Medium-sized white terrier with brown spots. Right common carotid, 4-5 mm. in diameter, exposed, divided and sutured as in foregoing experiments. Suture only moderately satisfactory. Considerable leakage, which soon ceased. No constriction of artery. Pulsation of artery distal to suture as strong as that proximal to suture. Right external jugular, 6-8 mm. in diameter, divided and sutured. Suture very satisfactory, no leakage. Tissues approximated over vessels with fine silk sutures. Subcutaneous silk sutures. Silver foil dressing. Crinoline bandage.

May 23, 1906.—Bandage removed. Healing per primam. Dog in good condition.

June 10, 1906.—Dog in excellent condition. Anæsthetized and vessels exposed. Very few adhesions about vessels at lines of suture. Vein not at all constricted. Section removed and lumen exposed. No thrombus formation. Intima very slightly roughened at line of suture. No constriction of artery. Intima perfectly smooth. Absolutely no thrombus (Fig. 7). Dog killed. Specimen in Kaiserling.

Histological examination.—Paraffin sections of the artery were stained with hæmatoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. The presence of the sutures distorts the sections and renders the microscopic study somewhat unsatisfactory. These sutures are surrounded by a few small round cells, epitheloid cells, and giant cells. The intima is smooth and lined by endothelial cells. As in the other cases, the angle between the everted ends of the inner elastic membrane is filled with a cellular fibrous tissue derived from the intima. This tissue contains numerous fine, new-formed elastic fibers which, toward the lumen, are thicker, denser, more wavy, and apparently take the place of the inner elastic membrane. While the scar is composed chiefly of connective tissue it is being rapidly invaded by muscle cells. The elastic fibers of the media and adventitia have as yet taken little part in the restoration of the arterial wall, but are very abundant next to the scar, occur in the peculiar whorls mentioned above, and are beginning to invade the scar. The adventitia is somewhat thickened and there is considerable thickening of the periadventitial tissues.

Expers. 31 and 32. Division and suture of left common carotid and left external jugular.—May 14, 1906.—Small black cur. Incision on left side of neck. Common carotid and external jugular exposed. Carotid, 4 mm. in diameter. Suture fairly satisfactory. Considerable leakage, which soon ceased. No extra sutures required. No constriction.

External jugular, 7 mm. in diameter. Suture satisfactory. No leakage. Slight constriction at suture. Some leakage into vein during suture, distal clamp holding poorly. Tissues over vessels sutured with fine silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

May 23, 1906.—Bandage removed. Healing per primam. Dog in fairly good condition.

June 10, 1906.—Dog in good condition, anæsthetized, and vessels exposed. Very little scar formation about artery, somewhat more about vein. No constriction of artery. Section of artery containing suture removed. No constriction. Intima smooth. Vein slightly constricted at suture. Section of vein removed and lumen opened. No thrombus. Very slight roughening of intima at suture. Specimens saved in alcohol (Fig. 8). Dog killed.

Expers. 35, 36, 37, and 38. Division and suture of both common carotids and both external jugulars.—May 23, 1906.—Large white and black cur. Both carotids and both external jugulars exposed through openings on either side of the neck. Carotids, 5 mm. in diameter. Jugulars, 6-7 mm. in diameter. Vessels divided and sutured with silk after Carrel's method. Both arterial sutures quite satisfactory. There was considerable leakage, which, however, soon ceased without extra sutures. No constriction. Venous sutures quite satisfactory. Very slight constriction. No leakage. Tissues over vessels sutured with fine silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

June 2, 1906.—Bandage removed. Wounds healed per primam.

June 10, 1906.—The dog, which had been sick for several days, died yesterday. Autopsy to-day: Vessels removed. No constriction of arteries. Intima smooth. Slight depression in intima at line of suture. Absolutely no thrombus formation. Specimens in Kaiserling (Fig. 9).

Left external jugular constricted and lumen occluded by small thrombus. Right external jugular also occluded. Organs of animal examined, apparently healthy. Death probably due to occlusion of both veins.

Expers. 41, 42, 43, and 44. Division and suture of both common carotids and both external jugulars.—June 1, 1906.—Medium-sized black and white cur. Both carotids and both external jugulars exposed through openings upon either side of the neck. Carotids, 5-6 mm. in diameter. Jugulars, 7-8 mm. in diameter. Ves-

sels divided and sutured after Carrel's method. Considerable leakage of left carotid requiring one extra suture. No constriction. Considerable leakage of right carotid also, but no extra suture was required. Suture of veins very satisfactory. No leakage. Very slight constriction. Subcutaneous silk sutures. Silver foil dressing. Crinoline bandage.

June 11, 1906.—Bandage removed. Wounds healed per primam. Dog in good condition.

June 18, 1906.—Dog has been sick for several days, died to-day. Autopsy: Vessels removed. Carotid sutures perfect. No constriction. Intima is quite smooth, but there is a slight depression at the line of suture. Lumen of right jugular considerably constricted by delicate cobweb-like bands. Left jugular occluded by stricture, probably due to organized thrombus, confined to line of suture. Specimens saved in Kaiserling (Fig. 10). Organs of dog apparently normal. Death probably due to poor venous circulation of head, following occlusion of veins.

B. Circular Arterio-venous Anastomoses.

Exper. 1. Circular anastomosis of the proximal end of the common carotid artery and the distal end of the external jugular vein.—February 21, 1906.—Small, curly-haired, brindle cur. The left common carotid artery, 5 mm. in diameter, and the left external jugular vein, 6-7 mm. in diameter, exposed and divided. Central end of carotid sutured to peripheral end of the jugular as in previous experiments. There was no leakage when the stream was turned on. The vein became distended until it was 8-9 mm. in diameter and pulsation could be felt in the vein near the head. Subcutaneous silver skin suture. Silver foil dressing. Crinoline bandage.

Feb. 24, 1906.—General condition good. Bandage removed. Wound looks clean. Whole left side of neck and head quite œdematous.

February 26, 1906.—Skin wound partly open. Marked pulsation in the jugular vein.

March 6, 1906.—Marked œdema of upper left neck.

March 21, 1906.—Wound almost healed. External jugular dilated and pulsating strongly.

April 3, 1906.—Dog seems well. Wound entirely healed. External jugular more than 1 cm. in diameter, pulsating vigorously. Loud systolic murmur heard over anastomosis and along the vein.

May 5, 1906.—Jugular as large as one's finger. Marked pulsation and loud murmur.

June 9, 1906.—Condition of animal good. Vein very large and thick. Murmur very loud.

June 26, 1906.—Dog anæsthetized and killed. Left external jugular vein distal to anastomosis much thickened and dilated, being perhaps 1 cm. in diameter. Right external jugular thinner and smaller. Both veins removed with connecting branch. On being opened after removal anastomosis was found to be perfect, the intima being absolutely smooth. The walls of the vein distal to the anastomoses were thickened and there were definite white placques in the intima. Slight dilatation behind the valves. Occlusion near beginning of small branch probably due to approximation of edges of valves. Thickening limited to unobstructed branch. Specimen in alcohol (Fig. 11).

Histological examination.—Paraffin sections of the vein a short distance distal to the anastomosis were stained with hæmatoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. The wall of the vein is about twice as thick as that of the corresponding vein on the opposite side. The tissues of the vessel wall seem less dense than normal, probably owing to a certain amount of œdema. All the coats of the vein are thickened, but the most marked thickening is in the intima and media. The thickening of the intima is by no means uniform for, in the regions corresponding to the whitish placques, seen in the gross specimen, it is four times as thick as in some other places. The endothelial cells lining the intima are short, thick, and contain large nuclei. The intima is composed of a fairly cellular connective tissue, which in places stains more poorly and contains fewer nuclei than elsewhere, but there is no atheromatous degeneration. The thickening of the media, which seems to be due to an increase in the interstitial connective tissue as well as to an increase in the size and number of its muscle cells, is less marked where the thickening of the intima is extreme. The thickening of the adventitia, which is fairly well marked, also varies somewhat with that of the intima. There, also, seems to be some increase in the thickness and density of the periadventitial tissues.

The inner elastic membrane is well seen. There are numerous fine elastic fibers in the thickened intima, especially in its deeper layers near the inner elastic membrane. They are also quite abundant at the edges of the intimal placques, but are not nearly so numerous in the body of these placques. While the elastic fibers are diminished in number in both the media and adventitia, the diminution is much more marked in the former.

Exper. 13. Circular anastomosis of the proximal end of the common carotid artery and the distal end of the external jugular vein.—March 19, 1906.—Small white terrier with brown spots. Left common carotid, 4 mm. in diameter, and left external jugular, 6 mm. in diameter, exposed and divided. Central end of carotid sutured to distal end of jugular by Carrel's method as in preceding experiments. No attempt to avoid intima. Suture very satisfactory. No leakage. Marked dilatation and pulsation of vein after removing clamps. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

March 28, 1906.—Bandage removed. Wound healed per primam. Strong pulsation in jugular vein. Thrill and bruit.

April 9, 1906.—There is a large swelling beneath lower jaw, more marked on the left, where fluctuation is felt, opened here and considerable pus evacuated. Marked pulsation in vein, systolic bruit and slight thrill.

May 5, 1906.—Marked thrill and loud murmur. Condition of dog good.

June 23, 1906.—Dog anæsthetized and left external jugular exposed. Vein pulsating vigorously, much dilated, 1.2 cm. in diameter, and apparently considerably thickened. On being opened, after removal, the walls of the vein were found to be twice as thick as those of the corresponding vein on the opposite side and the intima showed definite white placques, resembling those seen in arterio-sclerosis (Fig. 12). Specimen, along with opposite vein, saved in alcohol.

Histological examination.—Paraffin sections of the vein were stained with hematoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. Microscopic examination of these sections shows practically the same conditions as in the previous experiment. While all the coats of the vessel are greatly thickened, the thickening of the intima, especially in the regions corresponding to the white placques seen in the gross specimen, is very marked. The endothelial cells lining the intima are rather short and thick, but not so much so as in the preceding experiment. The intimal thickening is composed of fibrous tissue fairly rich in cells. In certain places this tissue contains fewer nuclei and stains more poorly, but no atheroma is present. The well-marked thickening of the media is due to an increase in its connective tissue, as well as to an increase in the number and size of its muscle cells. Where the intima is thicker the muscle cells seem fewer and are often separated by a considerable amount of fibrous tissue. The thickening of the adventitia is also well marked. There is a considerable increase in the elastic fibers of the intima, especially in the deeper portions near the inner elastic membrane, where a net-work of fine fibers is seen. As a rule the elastic fibers seem somewhat less abundant in the thicker

placques, but at their edges and in their deeper layers numerous fine elastic fibers are seen apparently invading them. The elastic fibers of the media and adventitia are diminished, but the diminution is more marked in the former.

Exper. 14. Anastomosis of central end of femoral artery and distal end of femoral vein.—March 26, 1906.—Large, straight-haired, brown dog. Left femoral artery and vein exposed in Scarpa's triangle and divided. Artery, 5 mm. in diameter. Vein, 6-7 mm. in diameter. Peripheral end of artery and central end of vein ligated. Central end of artery sutured to peripheral end of vein as in preceding experiments. No leakage. On turning on the current the vein became considerably distended and pulsation could be felt 7-8 cm. below point of anastomosis. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

March 28, 1906.—Leg very much swollen and œdematous, twice as large as the opposite one. Pulsation felt in vein 6 cm. beyond anastomosis. Dog looks rather sick.

March 31, 1906.—Dog lively, running around. Leg still much swollen. Wound apparently healing per primam. Loud systolic murmur along vein.

April 23, 1906.—Wound nicely healed. Loud murmur over vein. Marked pulsation felt in internal saphenous vein near the foot. Slight œdema of leg.

May 21, 1906.—Vein and its branches greatly dilated and pulsating actively. Marked thrill and loud murmur over anastomosis. Slight œdema of leg.

June 23, 1906.—Dog anæsthetized and anastomosis exposed. Vein distal to anastomosis pulsating actively, much thickened and dilated, being 1 cm. in diameter. The distal portion of the femoral artery was quite small and atrophic, apparently not performing the functions of a vein. On being opened after removal the anastomosis was seen to be quite smooth. Vein much thickened, intima thick and whitish (Fig. 13). Specimen in Kaiserling.

Exper. 45. Ligation of right femoral artery and vein.—April 9, 1906.—Small brown terrier. Right femoral artery and vein exposed in Scarpa's triangle and both ligated. Small branches of both vessels also tied. Wound closed with silk. No dressing.

April 20, 1906.—Wound healed per primam. Dog lively. No evidence of gangrene of leg.

This experiment was done as a control to those in which the central end of the femoral artery is sutured into the distal end of the femoral vein, to see whether simultaneous ligation of both femoral vessels will cause gangrene. Of course, one cannot draw definite conclusions from one experiment.

Exper. 19. Anastomosis of central end of femoral artery and distal end of femoral vein.—April 9, 1906.—Medium-sized white terrier with yellow spots. Right femoral vessels exposed in Scarpa's triangle and divided. Distal end of artery and proximal end of vein ligated. Central end of artery anastomosed to the distal end of vein. Slight leakage which soon ceased. On removing clamps vein became quite tense and pulsated vigorously. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

April 11, 1906.—Dog lively. Little, if any, œdema of leg.

April 21, 1906.—Wound healed per primam. No pulsation felt in vein. No bruit heard. Thrombus doubtless present. Leg in good condition.

June 10, 1906.—Dog anæsthetized and killed. Anastomosis occluded by organized thrombus extending 1 cm. into artery and vein.

Exper. 26. Crossed anastomosis of femoral artery and vein.—May 2, 1906.—Medium-sized black and white cur. Right femoral vessels exposed in Scarpa's triangle, dissected free for a distance of 6 cm. Artery, 5 mm. in diameter. Vein, 6 mm. in diameter. Both vessels divided between clamps and the central end of the artery sutured to the distal end of the vein and the distal end of artery to the central end of vein. Sutures unsatisfactory on account of the great tension which necessitated flexion of the leg and rough handling of vessels. Thrombosis expected. When the clamps were removed the distal end of the vein became distended, pulsated, and assumed the functions of an artery. There was apparently no return of venous blood through the distal portion of the artery. Tissues over vessels approximated with fine silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage. Three hours after operation marked pulsation could be felt in the internal saphenous vein near the foot.

May 3, 1906.—Dog died rather suddenly this morning, about 24 hours after operation. Anastomosis of central end of artery and distal end of vein occluded by thrombus, beginning sharply at suture and extending 1 cm. into vein, which was considerably dilated. Several very small thrombi adherent to the suture uniting the distal end of the artery and the central end of the vein. Organs examined, but nothing further found to account for death.

Exper. 30. Anastomosis of central end of femoral artery and distal end of femoral vein.—May 9, 1906.—Large brown setter. Left femoral vessels exposed. Distal end of artery and central end of vein ligated. Central end of artery sutured to distal end of vein by Carrel's method as in preceding experiments. Slight leakage, controlled by one extra suture. On turning on current the distal end of the vein bellied out and pulsated actively. Branches of vein gradually filled with arterial blood as the valves were forced. Two hours after operation pulsation was well felt in the internal saphenous vein near the foot. Tissues over vessels approximated with fine silk. Subcutaneous silk suture. Silver foil dressing. Collodion. Crinoline bandage.

May 14, 1906.—Dog looks sick. Entire left leg much swollen, quite cold. No pulsation felt in vein distal to suture.

May 15, 1906.—Dog dead. Autopsy: Left leg gangrenous. Infection about wound. Thrombus present, filling lumen of vein, beginning at suture and extending 1.5 cm. into vein.

Exper. 33. Circular anastomosis of left common carotid artery and left external jugular vein.—May 14, 1906.—Small yellow cur. Left external jugular and common carotid exposed. Vein, 6-7 mm. in diameter. Artery, 4-5 mm. in diameter. Vessels divided. Distal end of artery and proximal end of vein ligated. Proximal end of artery sutured to distal end of vein by Carrel's method. Considerable leakage, which soon ceased. No extra suture required. Marked dilatation and pulsation of vein when current was turned on. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

May 23, 1906.—Healing per primam. Marked pulsation, thrill, and murmur over vein distal to suture.

June 23, 1906.—Animal in good condition. Active pulsation in vein. Loud murmur and marked thrill. Anæsthetized and specimen removed, along with corresponding portion of the opposite vein. Anastomosis perfect. Vein distal to suture considerably dilated and somewhat thickened. Specimen in Kaiserling (Fig. 14).

Histological examination.—Paraffin sections of the vein were stained with hæmatoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. The changes in the vein are much less marked than those in the veins of experiments 1 and 13, owing not only to the shorter time elapsing after the operation, but probably to some extent to the large amount of periadventitial thickening in this case, which probably supported the venous wall. The intima which is more or less uniformly thickened, is lined by short, thick, almost cuboidal cells. The thickening of the intima is due to an increase in the subendothelial tissues. The thickening of the media is slight, but the muscle cells seem somewhat larger than normal. There is little, if any, thickening of the adventitia, but the periadventitial tissues are quite thick and dense. As yet there are no noticable changes in the distribution of the elastic tissue fibers.

Exper. 40. Circular anastomosis of the central end of the common carotid artery and the distal end of the external jugular vein.—May 28, 1906.—Very small white terrier with brown spots. Left external jugular and common carotid exposed. Artery, 4 mm. in diameter. Vein, 6 mm. in diameter. Distal end of carotid and proximal end of jugular ligated. Proximal end of carotid sutured to distal end of vein as in previous experiments. No leakage. Marked dilatation and pulsation of vein on removing clamps. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

June 16, 1906.—Wound healed per primam. Vein much dilated and pulsating actively. Loud murmur and marked thrill present.

June 23, 1906.—Dog has escaped from paddock, is lost.

C. Lateral Arterio-venous Anastomosis.

Exper. 2. Lateral anastomosis of femoral artery and vein.—February 21, 1906.—Large black and brown hound. Left femoral vessels exposed in Scarpa's triangle. Artery, 5 mm. in diameter. Vein, 5-6 mm. in diameter. Numerous branches divided and ligated. Vessels thus well freed and clamps applied. Small oval openings 1 cm. long made in vessels. Four primary sutures applied and joined by continuous sutures. No leakage when clamps were removed. Vein became considerably dilated. Marked thrill could be felt in vein and loud murmur could be heard at some distance from animal. The red arterial stream could be seen through the thin walls of the vein, rushing into the vein and for the most part returning immediately to the heart with the venous stream. Wound closed with silk and subcutaneous silver. Silver foil dressing. Collodion. Crinoline bandage.

February 24, 1906.—General condition good. Considerable œdema of leg. Superficial veins dilated. Marked thrill.

February 26, 1906.—Wound healed per primam. Slight œdema of leg. Vein near anastomosis markedly dilated. Thrill seems less intense. Loud humming-top murmur can be heard as far as knee.

March 13, 1906.—Intense thrill. Loud murmur heard well below knee.

March 28, 1906.—Dog in good condition. No œdema of leg. Femoral vein moderately dilated. Branches of vein considerably dilated and pulsate. Marked thrill and loud humming-top murmur.

April 2, 1906.—Dog has disappeared, apparently stolen.

Exper. 15. Lateral anastomosis of femoral artery and vein.—March 26, 1906.—Large, curly-haired, brown dog, apparently very old. Left femoral vessels exposed. Artery, 6 mm. in diameter. Vein, 7 mm. in diameter. Several branches divided and ligated and vessels freed for a distance of 5-6 cm. Clamps applied. Oval openings about 8 mm. long made in vessels 5 cm. below Poupart's ligament. Four primary sutures applied. Continuous sutures between these as in previous experiment. All coats of artery and vein included in suture. No leakage. Slight constriction of artery. Vein became considerably distended. Marked thrill. Loud murmur, audible to naked ear. Tissues over vessels approximated with fine silk. Subcutaneous silk suture. Silver foil dressing. Collodion.

March 28, 1906.—General condition good. Considerable œdema of leg. Marked thrill and loud murmur present.

March 31, 1906.—Dog looks sick. Some bloody discharge from upper extremity of wound. Murmur and thrill present, but not so intense as at last note.

April 2, 1906.—Considerable bloody discharge from wound and some evidence of hæmatoma. Murmur can still be heard about point of anastomosis, but is much less distinct and apparently systolic in time. Very slight thrill.

April 3, 1906.—Dog very sick. Large hæmatoma present. Suture evidently leaking. Animal killed.

Exper. 18. Lateral anastomosis of femoral artery and vein.—April 9, 1906.—Medium-sized white and black hound bitch. Left femoral artery and vein exposed for a distance of 3-4 cm. and numerous branches ligated. Artery, 4 mm. in diameter. Vein, 5 mm. in diameter. Clamps applied. Small elliptical openings made in vessels 4 cm. below Poupart's ligament. Four tension sutures applied, connected by continuous sutures penetrating all the coats of the vessels. No leakage. Some constriction of artery, but pulsation of artery distal to suture remained strong. The arterial blood rushed into vein through the anastomosis and divided into two parts, the one returning to the heart, the other distending the vein for a short distance distal to the anastomosis. This distance gradually increased and the branches of the vein were filled with arterial blood as the valves were forced. Loud murmur and marked thrill. Wound closed with silk. Silver foil dressing. Crinoline bandage. Dog has distemper, does not look very strong.

April 11, 1906.—Dog lively. Very slight œdema of leg.

April 13, 1906.—Bandage removed. Wound looks clean. Loud murmur and marked thrill present.

April 14, 1906.—Murmur has disappeared. Thrombosis has probably occurred.

April 19, 1906.—Wound slightly infected, open at upper extremity.

May 5, 1906.—Wound healing by granulation. No thrill. No murmur.

June 23, 1906.—Dog anæsthetized and specimen removed. Femoral artery near anastomosis thrombosed for a distance of 2-2.5 cm. and converted into a fibrous cord. Vein patent. Lumen little, if at all, reduced in size. Slight depression in intima of vein indicating location of previous opening.

Exper. 27. Lateral anastomosis of femoral artery and vein.—May 2, 1906.—Large, curly-haired, black dog. Lateral anastomosis of left femoral vessels about 5 cm. below Poupart's ligament. Same technic as that used in foregoing experiment, except that the vein was not loosened up as much. Suture very satisfactory. No leakage. Considerable constriction of lumen of artery. When the current was turned on the bright arterial blood could be seen to enter the vein, the greater part returning immediately to the heart, the other making its way a short distance downward in the vein. Marked thrill. Loud murmur. Artery, 5 mm. in diameter. Vein, 6 mm. in diameter. Well-marked pulsation in artery distal to anastomosis. Tissues over vessels approximated with silk. Subcutaneous silk suture. Silver foil dressing. Crinoline bandage.

May 12, 1906.—Wound healed per primam. Marked thrill. Loud humming-top murmur.

June 1, 1906.—Thrill and murmur present, but not so marked as formerly.

June 23, 1906.—Thrill and murmur have disappeared. Dog anæsthetized and specimen removed. No thrombosis in either vessel. Intima smooth, with exception of slight depression indicating site of previous opening, which has closed. Anastomotic opening in this and foregoing case should have been made larger.

D. Transplantation of Arteries and Veins.

Exper. 3.—Excision and replantation of a section of the femoral artery.—March 5, 1906.—Small yellow cur. Left femoral artery, 4 mm. in diameter, exposed and several branches ligated. Section of artery, 2-2.5 cm. in length, removed and replanted, the sutures being done after Carrel's method. The excised portion contracted a great deal, the resulting tension making the suture rather difficult. Slight leakage, which soon ceased. Active circulation through artery after removal of clamps. On account of the considerable handling of the artery there seemed some danger of thrombosis. Tissues over vessels approximated with silk. Subcutaneous silk suture. No dressing.

March 13, 1906.—General condition of animal fairly good. Some swelling about wound, which is doubtless infected. Artery undoubtedly thrombosed. No pulsation felt.

March 17, 1906.—Wound entirely healed. No pulsation felt in femoral artery.

June 23, 1906.—Animal anæsthetized. Replanted artery thrombosed and converted into fibrous cord.

Exper. 6. Transplantation of a section of the external jugular vein into the femoral artery.—March 7, 1906.—Medium-sized white terrier with brown spots. Left external jugular vein exposed and 2.5 cm. thereof excised. Left femoral artery exposed and 1 cm. thereof excised. Vein, 6 mm. in diameter. Artery, 5 mm. in diameter. Section of vein sutured between ends of femoral artery by Carrel's method. When the arterial stream was turned on there was a slight leakage at the proximal suture, which was controlled by one extra suture. The vein became quite tense, about 8 mm. in diameter, and a water-hammer-like pulse could be felt in it. Circulation apparently active. Subcutaneous silk suture. No dressing.

March 9, 1906.—Transplanted vein feels very hard. No pulsation felt in it or in femoral artery below. Thrombosis probably present.

March 17, 1906.—Wound healed per primam. No pulsation in transplanted vein.

June 10, 1906.—Dog anæsthetized. Transplanted section of vein thrombosed and converted into fibrous cord.

Exper. 39. Transplantation of a section of external jugular vein into the common carotid artery.—May 28, 1906.—Small yellow cur. Incision in the left side of the neck. Common carotid, 4 mm. in diameter. External jugular, 6 mm. in diameter. Section of jugular vein 3 cm. long excised and transplanted between the cut ends of the carotid artery. On removing the clamps there was no leakage, the transplanted vein became considerably distended and pulsated actively, as did the common carotid artery distal to the suture. Slight thrill in vein. Subcutaneous silk culture. Silver foil dressing. Crinoline bandage.

June 10, 1906.—Dog in good condition. Bandage removed. Healing per primam. Pulsation felt in the transplanted vein.

June 23, 1906.—Dog anæsthetized. Transplanted vein exposed. Vein considerably dilated, 8-9 mm. in diameter, and thickened, pulsating vigorously. Specimen removed and opened. Both sutures quite smooth. Intima of vein whitish, evidently considerably thickened. Specimen in Kaiserling (Fig. 15).

Histological examination.—Sections of the vein were stained with hæmatoxylin and eosin, Van Gieson's stain, and Weigert's elastic tissue stain. The intima is lined by flat endothelial cells. The thickening of the intima, which is due to an increase in the subendothelial tissue, is fairly uniform. The media is considerably thickened, the thickening being due to an increase in the interstitial connective tissue rather than to any marked increase in the size or number of the muscle cells. While the adventitia is somewhat thickened there is a striking increase in the thickness and density of the periadventitial tissue. There seems to be an increase in the elastic tissue of the intima and a diminution in the elastic tissue of the media and adventitia.

E. Partial Occlusion of Vessels by Suture.

Exper. 34. Partial occlusion of the aorta.—May 14, 1906.—White and yellow shepherd. Abdominal incision. Aorta exposed a short distance above its bifurcation and its lumen narrowed by several through and through sutures. After the suture was completed the pulsation distal to the suture was considerably diminished. Wound closed with silk. No dressing.

May 23, 1906.—Dog in good condition. Healing per primam.

June 23, 1906.—Dog anæsthetized and specimen removed. Lumen of aorta diminished to half its normal size by the sutures. Many of the sutures projected into the lumen and were covered with a thin layer of organized fibrin. Specimen in Kaiserling.

F. Transplantation of Organs.[1]

Exper. 46. Transplantation of the thyroid gland.—January 31, 1906.—An incision was made on the left side of the neck of a large black and brown hound. The thyroid gland was dissected out, but was left attached to the carotid artery and to a vein, 3 mm. in diameter, leaving its lower pole. After being washed out with salt solution the gland was removed, along with a portion of the carotid artery and the small inferior vein, and transplanted into the neck of a somewhat smaller black and white cur, which had been prepared for it. Carotid was sutured to carotid and the small inferior vein to the internal jugular, which was of about the same size. The suture of the arteries was satisfactory, but the suture of the veins was quite unsatisfactory on account of their small size. Circulation of gland doubtful. Wound closed with interrupted silk sutures. No bandage.

February 19, 1906.—Dog well. Wound healed per primam. Weight, 33 pounds.

February 26, 1906.—Dog in good condition. Weight, 38 pounds.

May 3, 1906.—Dog anæsthetized and examined. Vessels thrombosed. No trace of gland found.

Exper. 47. Transplantation of the thyroid gland.—February 7, 1906.—Thyroid removed from the left side of the neck of a large, curly-haired, brown dog. Portion of carotid removed with the thyroid. There was a vein, 4 mm. in diameter, passing medially from the lower pole of the thyroid. This vein was used for subsequent suture. Gland washed out with salt solution and completely blanched, then transferred to a small white terrier already prepared. Carotid sutured to carotid; median vein to the external jugular. The carotid suture leaked somewhat, one extra suture being required. The clamp on the artery was now removed and there was considerable bleeding through the gland while the vein was being sutured. Venous suture fairly satisfactory in spite of the disproportion between the veins. The blood passed through into the external jugular as could be shown by the great distension of the external jugular when pressed upon. Skin closed with interrupted silk sutures. No bandage.

February 13, 1906.—Wound broken open. Gland lost. Thrombosed end of carotid seen in wound. Faulty asepsis.

Exper. 48. Transplantation of the thyroid gland.—February 14, 1906.—Thyroid removed from the left side of the neck of a very large, curly-haired, black dog. Internal jugular vein very small, 3-4 mm. in diameter. No median vein. The dog died shortly after the operation was begun. Gland hastily removed after death, along with portion of the common carotid and internal jugular. Gland washed clean and left in salt solution while the other dog was being prepared. Gland transferred into the neck of a small white terrier with brown spots on the head. Carotid sutured to carotid; internal jugular to external jugular. Suture in artery leaked considerably, requiring one or two extra sutures. Considerable disproportion in both arteries and veins, especially in the veins. Venous suture fairly satisfactory. Circulation in the gland good. Subcutaneous silver suture. Silver foil dressing. Crinoline bandage.

February 26, 1906.—Wound entirely healed. The dog is lively, but very thin. The transplanted thyroid can be easily felt.

March 13, 1906.—Dog still very thin. Transplanted thyroid can be readily palpated.

March 17, 1906.—Considerable swelling about the gland, soft and fluctuant.

March 21, 1906.—Dog anæsthetized and operated upon. Swelling found to be a collection of turbid fluid surrounded by scar

[1] These experiments were done by Dr. W. G. MacCallum and myself.

tissue. No remains of thyroid gland found. Small necrotic pieces of transplanted carotid present.

Exper. 49. Transplantation of the thyroid gland.—February 19, 1906.—Thyroid gland removed from the left side of the neck of a large brown dog, along with a portion of the carotid artery and median, inferior vein, which was fairly large, 4 mm. in diameter. Gland washed out with salt solution and transferred into the neck of a small white cur. Carotid sutured to carotid, the suture being quite satisfactory. Median vein sutured to the external jugular; venous suture unsatisfactory on account of the great disproportion in the size of the veins, did not allow very free passage of blood. Subcutaneous silver suture. Silver foil dressing. Crinoline bandage.

February 26, 1906.—Wound broken open, granulating well. Gland not exposed, muscles apparently having healed together over the gland.

March 3, 1906.—Dog anæsthetized. Large hæmatoma under wound in neck, doubtless due to rupture of the carotid suture. Thyroid doubtless necrotic, not found. Remains of transplanted vessels found, also soft and necrotic. No pus present.

Exper. 50. Transplantation of the thyroid gland.—February 26, 1906.—Thyroid gland along with portions of the carotid artery and a small vein leaving its lower pole removed from a large yellow setter, washed out with salt solution and transplanted into Scarpa's triangle of a small white terrier with black ear. Carotid artery sutured to the femoral artery and the inferior vein to the femoral vein. Sutures very satisfactory. No leakage. Circulation quite satisfactory for a time, the small arteries of the gland pulsating actively; later the circulation became more sluggish. Skin closed with interrupted silk sutures. Silver foil and collodion dressing.

March 3, 1906.—Dog anæsthetized. Left leg œdematous and gangrenous. Artery and veins of gland thrombosed, thrombi extending into the femoral vessels. Transplanted thyroid necrotic.

Exper. 51. Transplantation of the thyroid gland.—February 28, 1906.—Remaining thyroid removed from the neck of the large, curly-haired, brown dog used in experiment 47. Thyroid not hypertrophied. Portion of the carotid artery and inferior median vein, 3-4 mm. in diameter, removed with gland. Gland washed out with salt solution and transplanted into the abdomen of a small white cur with black spots. Carotid artery sutured to the common iliac artery and the median vein of the thyroid to the common iliac vein. Arterial suture fairly satisfactory. Slight constriction of the vein at the site of suture. Circulation in the gland quite active when the abdomen was closed.

March 10, 1906.—Dog seems well. Wound entirely healed with the exception of a small granulating sinus at its posterior extremity.

March 12, 1906.—Dog very sick. Considerable discharge of dark blood from the sinus mentioned above. Killed with choloroform and examined. Sinus found to lead down to a large cavity in the region of the transplanted thyroid, filled with blood-clot. Thyroid not found, doubtless very necrotic. Remains of thyroid vessels found, filled with thrombi extending into the iliac vessels. Tissues of leg in good condition, no gangrene.

Results.—The common carotid artery was sutured thirteen times. All of the sutures were perfectly successful and in no case was there the slightest evidence of thrombus formation. The femoral artery was sutured twice, thrombosis occurring both times as a result of wound infection. The external jugular vein was also sutured thirteen times, ten of the sutures being successful.

Microscopic examination of the arterial sutures at periods varying from twenty-eight to eighty-two days after the operation shows that there is a gradual restoration of the artery at the site of suture and that with the exception of the inner elastic membrane, all the elements of the vessel wall are probably regenerated. The sections of the thin-walled veins which were obtained were so distorted by the presence of the silk sutures that they were of little value for microscopic study.

The common carotid artery was sutured to the external jugular vein four times, all being successful. After the suture the veins became distended and pulsated vigorously; a marked thrill could be felt in the veins and a loud murmur heard over them. Examination of the veins one to three months after the operation showed a marked dilatation of these vessels, a thickening of their walls, and in some there were interesting placques in the intima, suggesting the changes seen in arterio-sclerosis. Microscopic examination of the walls of the veins revealed changes very analagous to those found in the walls of arterio-sclerotic arteries. In the vein of experiment 13 (see Fig. 12) the following condition was found: While all the coats of the vessel were greatly thickened, the thickening of the intima, especially in the regions corresponding to the white placques seen in the gross specimen, was very marked. The endothelial cells lining the intima were short and thick. The intimal thickening was composed of fibrous tissue fairly rich in cells. In certain places this tissue contained fewer nuclei and stained more poorly, but no atheroma was present. The thickening of the media was due to an increase in the interstitial connective tissue as well as to an increase in the size and number of its muscle cells. Where the intima was thicker the muscle cells seemed to be fewer and were separated by a considerable amount of connective tissue. The thickening of the adventitia was also well marked. There seemed to be a considerable increase in the elastic fibers of the intima, especially in the deeper portions near the inner elastic membrane, where a net-work of fine fibers was seen. In general, the elastic fibers seemed somewhat less abundant in the thicker placques, but at their edges and in their deeper layers numerous fine elastic fibers were seen, apparently invading them. The elastic fibers of the media and adventitia were diminished, but the diminution was more marked in the former.

The central end of the divided femoral artery was sutured to the distal end of the divided femoral vein four times. One case was successful; in the others thrombosis occurred. In the successful case the leg became very much swollen after the operation and in two days was twice as large as the opposite one. The swelling gradually subsided but never entirely disappeared. The femoral vein became much dilated and marked pulsation could be felt in the saphenous vein near the foot. Examination three months after the operation showed a marked dilatation and thickening of the wall of the vein. The distal portion of the femoral artery was small, atrophic, and did not seem to be performing the functions of a vein.

In four animals a lateral anastomosis of the femoral artery and vein was made. In all the cases the immediate result was

quite satisfactory; on turning on the blood stream there was no leakage, the vein became considerably distended, a thrill could be felt in it near the point of anastomosis and a humming-top murmur could be heard at some distance from the animal. The red arterial stream could be seen through the thin-walled vein, rushing into the vein and for the most part returning immediately to the heart. In only one of the animals, however, did the anastomosis remain patent, a marked thrill and loud murmur being present five weeks after the operation when the animal escaped from the paddock and was lost. In the second animal the murmur and thrill persisted for four weeks and then disappeared, examination a few weeks later showing that the anastomotic opening had healed, but that the vessels had remained patent. In the third animal, whose wound became infected, the thrill and murmur lasted only four days; examination two months later showed a thrombosis of the artery, the vein remaining unobstructed. In the fourth case the thrill and murmur persisted five or six days, death occurring on the eighth day after operation from secondary hæmorrhage.

Excision and replantation of a section of the femoral artery was done once, but thrombosis occurred. Transplantation of a section of vein into an artery was tried twice. In one instance a section of the external jugular vein was transplanted into the common carotid artery with perfect success. Examination of the specimen (see Fig. 15) twenty-six days after the operation showed considerable dilatation and thickening of the transplanted vein and the microscopic study of the vein revealed a condition very similar to that described above, resulting from the end to end anastomosis of the carotid artery and jugular vein. In the other case a section of the external jugular vein was transplanted into the femoral artery, but thrombosis resulted in a few days.

Transplantation of the thyroid gland was done six times, but none of these were successful. The failure of these experiments may be attributed to the small size of the inferior thyroid vein, whose diameter rarely exceeded two or three millimeters, and to the fact that the transplantations were undertaken before we had made any experiments with simple vascular sutures.

In reviewing our experiments we find that of thirty-one experiments upon the vessels of the neck twenty-eight were successful, whereas of twelve experiments upon the femoral vessels only two were entirely successful. This discrepancy is not difficult to explain. Wounds in the neck are inaccessible to the dog's teeth, and can be readily bandaged, the wounds being thus kept clean and dead space obliterated. In the groin, however, it is very difficult to apply a bandage which will remain in place, obliterating the large dead space which is so apt to be present and preventing movements of the leg which interfere materially with a successful vessel suture.

The results show conclusively that completely divided vessels can be sutured with almost uniform success, when the aseptic technic is good. The intima can be included in the suture with impunity, the application of the suture being thus greatly facilitated.

Nearly all experimenters with the suture of blood-vessels have called attention to the need of a very perfect technic. I wish also to emphasize this point, for I consider infection by far the most important factor in producing thrombosis after vascular sutures. I think, as Carrel does, that there may be minor grades of infection, which, although allowing per primam healing of the wound, may be sufficient to produce thrombosis of the sutured vessels.

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BOSTON MEDICINE ONE HUNDRED YEARS AGO AND A NOTABLE PHYSICIAN OF THE LAST CENTURY.[1]

By J. G. Mumford, M. D.

In 1807 but four young men were graduated in medicine from the Harvard school, and received the degree of M. B. Those were pleasant times in which to live in Boston. The town was still a small town, not yet raised to the dignity of a city—a town of 25,000 inhabitants, about a quarter the size of our modern Cambridge, or with a population one-twentieth of what Baltimore now contains. We have abundance of light on the life of the period. Men of letters were concerned in writing history, and the journals and epistles of the day abound in descriptive story. The Harvard Medical School was 25 years old, and the original three professors, John Warren, Benjamin Waterhouse, and Aaron Dexter still exercised their professorial functions. It was a time of comfort and activity in the commercial and academic worlds. Society was busy in charity, and spoke good will; while the temper of the people was not different from what it had been more than a hundred years earlier when Increase Mather wrote of Boston that "for charity, he might indeed speak it without flattery, this town hath not many equals on the face of the earth." Some fond optimists still maintain the boast.

In those days of 100 years ago, the respectable and influential people of the town—as the old writers call them—were actively exercised in forming and carrying on all sorts of educational, philanthropic, and literary enterprises, as their descendants do to this day. The Massachusetts Medical Society, the most potent and far-reaching of State medical societies, was making itself felt in the uplift of the profession, and among its active and important promoters were such well-known men as Holyoke, the two Warrens, Jackson, Gorham, and Jacob Bigelow; the Medical School was developing as an important department of Harvard University; the Massachusetts Historical Society was in the 14th year of its distinguished career; libraries such as the Columbian, the Anthology Reading Room—which subsequently became the Boston Atheneum—and the Boston Library Society were beginning to gather those great collections which to-day are the pride and solace of scholars; the Massachusetts Humane Society, the Massachusetts Charitable Association, the Charitable Mechanic Association, the Boston Dispensary, the Boston Female Asylum, and a dozen other cognate organizations were flour-

[1] Read before the Johns Hopkins Historical Club, February 11, 1907.

ishing in a vigorous young life. The Massachusetts General Hospital was in process of inception at this time, though 14 years were to elapse before it was opened to patients.

Writers tell of a charming society living in the midst of an unusually beautiful environment. The country of eastern Massachusetts was nearly 200 years settled, and in those days, before railroads and steamboats existed, when connection with other states was by post road and coasting vessels, Boston seemed a remote and detached town. It was then an important shipping port. The vessels of its merchants sailed for the old countries of Europe, the south seas, and India, so that it had built up within itself a rather self-centered population; a community old in years as American communities then went, with long-established customs, and a widely cultivated country, after the turmoil of the Revolution. Be it remembered of Boston society, as with the society of other ancient colonial towns, that the Revolution had put an end almost to the old time dignified life. Representative families, largely, were Tories, and left the country when Boston fell before the arms of Washington. A new society grew up and new men appeared as eminent citizens, so that it was not until a second generation began to develop that a renewing of the former stability became apparent. That was the condition in the early years of the last century. The Revolution and the infusion of new, restless, democratic persons into the affairs of the place, tinctured though such persons were with many of the ideas and prejudices of former times, developed an active, progressive and interesting assemblage of people. In 1807 the growth of the new West had hardly begun to take on that fury of interest and activity which characterized it in the next generation. The old States themselves were thinly settled still, and eastern Massachusetts, isolated and far removed from other great centers, went about its business in self-confident and thorough fashion.

There was one exception as yet to this self-confidence, and that exception was in the education of physicians. Massachusetts had always abounded in doctors. The medical profession was a favorite profession there in colonial days, but the best of the doctors had to look beyond the colony for their education. Many of them went to London and Edinburgh, but more flocked to the Philadelphia school. The foundation of the Harvard Medical School, in 1782, by no means put a stop to these Philadelphia journeys, for it took many years to bring the Harvard school up to the Philadelphia standard. Many young men contented themselves still with completing their professional studies in the offices of some licensed practitioner; a few took a two-term course at the Harvard school, but the more ambitious travelled away to Europe and to Philadelphia to complete their studies and receive the doctor's degree. In those days Philadelphia had this lead over Boston in the advantages it offered medical students, that it provided abundant clinics at the old Pennsylvanian Hospital. At Harvard there was no clinic worth the name. A few patients were shown weekly at the ancient Boston almshouse, but the school proper was in Cambridge, a two hours' journey from Boston then, and the instruction given in Cambridge was altogether didactic. I am not sure but what the total instruction of those times was extremely good instruction. In a measure we have returned in these days to a similitude of the ancient method. Largely the instruction was personal. A group of two or three young men studied under and received the active directions of an experienced physician, and supplemented the knowledge of practice thus acquired, by the didactic lectures of Warren and Waterhouse in Cambridge.

A younger generation as it came along, however, was dissatisfied with the old method. The young men were convinced that a medical school two hours from the metropolis could not flourish; and well-equipped physicians returning from London and Philadelphia urged the importance of re-establishing properly the somewhat somnolent Harvard school. We must remember, however, that the views of a community of 100 years ago differed materially from modern views. The laity feared great bands of medical students, regarding them as vandals; while practicing physicians had a natural feeling of jealousy of a medical school, fearing that it would detract from their own importance as educators, and would raise to an unduly prominent position in the profession the teachers in the school. If the development of Boston medicine had depended upon a majority vote, uninstructed by the enlightened few, there can be no doubt that the Harvard school would have languished obscurely in Cambridge for another generation, or would have disappeared; but fortunately some in the community were coming to take broader views, through the stimulus of such general educational enterprises as I have already mentioned, and through the urging of young enthusiasts fresh from the hospitals of Europe. Of the latter class, John Collins Warren and James Jackson, six years established in practice, were the most active; and Warren's father, John Warren, the honored professor of surgery, lent himself earnestly to the forward movement. Curiously enough his colleague, Benjamin Waterhouse, professor of practice, himself a product of European schools, opposed bitterly, and to the end of his career as a teacher, the plan for medical school expansion. He was a didactic teacher, little given to the arts of clinical instruction, and he seems to have feared the comparison and rivalry of an association with the proposed new professor of clinical medicine, young James Jackson. But liberal views came eventually to prevail through much travail and grievous heart-burning. Waterhouse left nothing undone which might obstruct progress. He joined with others in an endeavor to anticipate the Harvard movement, by establishing in Boston a rival school of medicine to be known as the College of Physicians; and when that endeavor failed he attempted to damage his colleagues by publishing what the corporation of the college designated as false, scandalous, and malicious libels upon the other professors, which had a tendency to injure their characters, offend their feelings, and diminish their usefulness in the university. The outcome of it all was that Waterhouse was forced to resign, after the school had been removed to Boston, which was accomplished in 1810.

Then the faculty was reenforced and reorganized, with such strong and notable representatives as I have already named.

So out of much turmoil, eager initiative and vigorous agitation on the part of a rising generation there was launched that small but effective school of medicine whose leaders, after struggling for academic reform in their youth, founded a great hospital in their prime, and in their old age revolutionized surgery by the discovery and introduction of ether anæsthesia.

You will perceive that it was an active, well trained, onward pressing generation, given much to that spirit of progress which prevailed throughout the land; but instructed also in ancient culture, in old-time kindliness, and with an enthusiasm, born of noble, national tradition and the philosophy of the day, for self-help, neighborly benefit and wide-reaching, catholic philanthropy.

We have heard much in recent years of the leaders who struggled in those days; let us turn the page and make ourselves acquainted with a joyous youth who grew up under such teachers, and put their teaching to the proof, Samuel Gridley Howe.

To the average American of to-day Samuel Howe is known, if at all, as the half-forgotten husband only of that distinguished veteran poetess Julia Ward Howe. Truly the pen is mightier than the sword. But he was himself the author of many good things for which American physicians, at least, should cherish him. It was a brilliant, impetuous, heroic nature; with a romantic career—full of lights and shadows, and strange contrasts. Pedantic folk used to call him "the apostle of freedom."

Howe was born in Boston in 1801, nine years before the Harvard school was removed from Cambridge. That was the year which saw the establishment in practice of Jackson and John C. Warren, and the new vaccination of Jenner introduced to these shores. There was little wealth in Howe's family, and the little there was dwindled sadly during the war of 1812; for his father, Joseph N. Howe, a ship owner and maker of cordage, trusted the federal government for naval supplies, and the government failed him. The unhappy merchant was brought nearly to ruin, and his family grew up in poverty. In spite of this there was money supplied for sending one of the boys to college, and Samuel was selected. He went to Brown, whence he was graduated in 1821, at the age of 20, a mature age for graduation in those days. The young man was an optimist born, enthusiast, and a lover of his kind. In his growing years he had seen develop in Boston those useful and pleasant enterprises of which I have told. In spite of commercial embargo and the English war, the buoyant spirit of the people continued to expand. With the fall of Napoleon and the general political reaction which set in throughout Europe, and in the face of the Holy Alliance with its far-reaching purposes, American patriots felt that the liberties of the race had been intrusted to them by a special providence. The Munroe Doctrine threw out a barrier against despotic aggression on these continents; and the youth of the land were growing up with a vivid enthusiasm for liberty, and with generous good will for the oppressed.

I have dwelt at some length on these qualities of our people in those times, because such were the qualities and sentiments which went far towards directing the impulses of young Howe, and moulding his career.

In the year of his graduating from college the insurrection in Greece against Turkish rule broke out, and thrilled the world. Probably no similar uprising ever awoke wider sympathy or provoked a more unanimous applause. Despotic governments trembled and frowned, but peoples rejoiced. Now, Howe was one of the people. While the senates of the old world were avoiding the ugly question of interference in Greece, and premiers were giving their secret instructions; while popular representatives at Washington were waving the flag and fulminating against tyrants, young Howe was pondering all these things. We know how the united uprising of the Greeks, though feebly directed and cruelly mismanaged, was able in three years to sweep away the contemptible opposition of intrenched Turkish misrule, and how the Porte was forced to turn to Egypt for aid against his revolted subjects. During those three years Howe was content to remain a spectator of the struggle, busied meantime with perfecting his education.

After his graduation from Brown he returned to Boston and entered as a medical student the office of Jacob Bigelow. At the same time he attended the lectures in the Harvard school, and the clinics at the Massachusetts General Hospital, finding as instructors Jackson, J. C. Warren, Parkman, and Ingalls. He must have been an interesting student—dear to the soul of such a splendid independent as Bigelow—acceptable even to the hard-headed, brilliant Warren, and his wise, great-hearted colleague Jackson. Such men could appreciate a promising student, and were foretelling an unusual future for Howe, when suddenly he astounded them and the Boston community by announcing that he was going to Greece. Even the restrained writers of the day flutter with protest and amazement when they tell of it. No one encouraged the rashness. The young man was called Byron-mad. No one encouraged him except one eminent man—Gilbert Stuart, the artist, now growing old, who faltered that his heart also was in the venture if only the times were still young for him. He helped Howe to go. He gave him money, got for him a letter from Edward Everett to an old friend in Greece, and with a quavering blessing sent him on his way.

So far it was all very fine, but our adventurer soon found his work cut out for him. When he left Boston, Greece was flushed with success, and preparing confidently for the final struggle. When he reached Napoli de Monembasia and had pushed on to the Greek headquarters, he found himself in a mob of terrified officials, without concert, screaming diverse counsels, savage, fatuous, ungoverned. Three years of horror had demoralised the Greeks, the best of whose leaders had been lost; though the people themselves had become hardy and trained to a cruel guerrilla warfare. In the autumn of 1824, when Howe joined these people, they were waiting for

the coming against them of a great Egyptian armament commanded by Ibrahim Pasha, one of the most vicious and clever reprobates in history; admiral of a considerable fleet, and captain of as blood-thirsty a set of cut-throats as ever twisted a neck. Four years later Howe published a short account of the proceedings of these gentry. Here are his own modest words:

"In the winter the much-dreaded expedition of Ibrahim Pasha, with the Egyptian army, landed at Molai. Attempts were made by the Greek government to get up an army to oppose them, and Mavrocordato accepted my offer to go with them as surgeon. The president and Mavrocordato came to the south of Peloponnesus with such forces as they could raise. At first there was an attempt to organize the army, and I attempted to create hospitals and to organize ambulances for the wounded. But after the capture of Navarino by the Turks, everything was thrown into confusion. Mavrocordato fled to Napoli. The dark day of Greece had come. All regular opposition of the Greeks was overcome. The Turks advanced fiercely and rapidly up the Peloponnesus. I joined one of the small guerrilla bands that hung about the enemy, doing all the harm they could. I could be of little or no use as surgeon, and was expected to divide my attention between killing Turks, helping Greeks, and taking care of myself. I was naturally very hardy, active and tough, and soon became equal to any of the mountain soldiery in capacity for endurance of fatigue, hunger, and watchfulness. I could carry my gun and heavy belt with yatagan and pistols all day long, clambering among the mountain passes, could eat sorrel and snails, or go without anything, and at night lie down on the ground with only my shaggy capot, and sleep like a dog."

Long afterward our gentle poet Whittier took Howe for his subject in "The Hero," and described an event which the hero himself recounts.

"I was by chance at Calamata after escaping from Navarino, when a sudden invasion of the Turks forced everyone to fly who could fly. I never shall forget the dreadful scene of confusion and distress, or my feelings, as I galloped through the town, accompanied by Ernest, a gallant young Swiss, for we passed many poor beings, old or sick, who were unable to fly on foot, and who stretched out their hands praying for God's sake that we would save them; but selfishness and the pressing danger made us turn a deaf ear, and think only of saving our own lives. We had left the town and were hurrying across the plain, which was occupied with fugitives, when I beheld a wounded soldier sitting at the foot of an olive tree, pale, exhausted, and almost fainting, but still grasping his long gun as if he meant to have a last shot at the expected foe; it was Francesco, who had been dreadfully wounded a few days before, and had staggered thus far from the temporary hospital at Calamata, on hearing the alarm. The poor fellow cast a supplicating look at us as we passed, but said not a word. That look cut me to the soul; had he presented his gun and demanded my horse, it would not have so moved me; I could not but turn my head after we passed him, and seeing him still looking after us, as I thought reproachfully, I pulled up my horse, and on calculating the distance, found I had time to gain the mountain; of course I turned back, mounted the poor fellow on my beast, and thus easily reaped the rich reward of his gratitude."

Time fails us; the narrative runs on for many pages. We know how the Egyptians over-ran the land, and how at last the fleets of England, Russia, and France were sent to intervene. By that time Howe had been three years in the Greek service, and was acting as surgeon-in-chief of the Greek fleet, a formidable collection of three frigates, two sloops and half a dozen wherries. On October 20, 1827, the strong armada of the European allies bottled up the Turco-Egyptian fleet in the harbor of Navarino, and annihilated it in an action as blood-curdling as the heart of Ibrahim himself could have asked. We are not told what part the Greek fleet, with their surgeon from Suffolk county, took in this action, but it is probable they were content to be spectators.

The slaughter of the Egyptians ended Turkish rule in Greece. Peace was established after much tribulation, and in the course of time a limited monarchy was set up with a Bavarian prince on the throne, as the figure-head of the western powers. Immediately after the battle of Navarino, however, Howe saw that the country was falling into a state of poverty and starvation. He was a humanitarian first, a physician and a soldier afterwards, so he resigned his office of surgeon-general, and posted back to Boston to proclaim the good tidings, and raise money for his suffering Greeks. The estimable ladies of Massachusetts listened over their teacups to the strange tales of the young Ulysses: they were moved to hold a fancy fair in Faneuil Hall; their husbands drew out their pocket-books, and Howe was despatched back to Greece with a ship-full of food and clothes. Then there was more trouble. The unhappy descendants of Plato and Pausanias had fallen to fighting among themselves, and sundry brigands with high-sounding titles attempted to relieve the missionary of his stores. Fortunately our old frigate Constitution happened to come along, and a file of marines from the vessel settled the dispute among the discordant Greek patriots. Howe distributed his good things, said good-bye to his mendicant comrades, and returned peacefully to his own country. The pathos and the humor of it all sift down to us through the century, and one fancies the picture: the ragged jabber of the poor, patched, huddled wretches, crouching among the ruins of departed Greece; each with a loaf of Yankee bread in one hand, a rusty dirk at the waist, smearing his face with farewell tears, and shouting to our departing hero as he steps smartly upon the deck of the neat cruiser, waves his hat and sails away for the smiling land across the polished sea.

In 1828, with Howe's return from Greece, the adventurous chapter of his life seemed to close; but other chapters and other adventures awaited him. He was an eager, enquiring soul; looking ever for something new, always appearing to tilt at wind-mills; but out of each bout bringing a measure of practical success, and hastening to new encounters. He was not content to tread in beaten paths, or gather laurels in familiar fields. While his contemporaries were earning snug

incomes in the old lines of practice, Howe was laying his own new lines, and attacking problems of disease hitherto held incurable. His works do live.

First he turned to the education of those born blind. A hundred years ago there was no future before these unhappy folk, save poverty, ignorance, and dependence, or suicide—and suicide even is not readily to be attained by one who cannot see. Howe was fortunate enough to secure the sympathy and support of Dr. John D. Fisher, a young man, one year his own junior—himself a philanthropist and with a private fortune. With Fisher's aid Howe took up the problem of teaching the blind and began his studies by visiting Europe again to investigate the Valentine Haüy methods then employed in Germany and France. In Europe he fell upon more adventures. France was in the throes of her second Revolution, and Howe reached Paris in time to see Louis Philippe seated insecurely upon the throne. Then Lafayette found him out and persuaded him to go on a mission to persecuted Poland in her death struggle with Russia; and to carry to the Poles supplies sent to them from their friends in America. So he became a filibuster in a small way. But the experience was a short one. The Poles were at the end of their tether. Howe visited them, accomplished his hazardous mission, and turned back to Berlin for the study of the blind. But the affair was not so simple, and he learned that free American citizens are not free to dabble casually in international politics. On the day of his arrival at the Prussian capital he was arrested by order of the government because of his Polish doings, was imprisoned and was left to ruminate for five weeks in a cell. But solitary confinement could not tame Samuel Howe. He secured some new German books on the education of the blind, and set about translating them. Years afterward the king of Prussia sent him a gold medal for his success in teaching Laura Bridgman, and the humorous philosopher tells how he calculated that the value of the medal offset exactly the charges for his fare while a guest in the German prison.

In 1832, when 31 years old, Howe settled down in Boston to that part of his life work for which he is most famous—the education of the blind. Happily Fisher stood by him; so did John Homans and Edward Brooks—names well known to-day in Massachusetts. Howe was full of ideas new to this country, and his active intelligence so supplemented the thoughts of others that he soon found himself a lonely pioneer in the work. Here is an interesting letter from a friend of Horace Mann to one of Howe's admirers.

"When we first became acquainted with Mr. Mann he took Mary (afterwards Mrs. Mann) and me to a small wooden house in Hollis street where, in the simplest surroundings, we found Dr. Howe with the first half-dozen pupils he had first picked up in the highways and byways. He had then been about six months at work, and had invented and laboriously executed some books with raised letters, to teach them to read, some geographical maps, and the geometrical diagrams necessary for instruction in mathematics. He had gummed twine, I think, upon cardboard, an enormous labor, to form the letters of the alphabet.

"I shall not, in all time, forget the impression made upon me by seeing the hero of the Greek Revolution, who had narrowly missed being that of the Polish Revolution also; to see this hero, I say, wholly absorbed, and applying all the energies of his genius to this apparently humble work, and doing it as Christ did, without money and without price. His own resources at this time could not have paid the expenses of his undertaking, with all the economy and self-denial he practiced. The fuller purse of his friend and brother, Dr. Fisher, assisted him. Soon after our visit to him, he brought out his class for exhibition, in order to interest people and get money sufficient to carry on the work on a larger scale. The many exhibitions given created a furor of enthusiasm, and Col. Perkins' great heart responded to the moving appeal. He now offered his fine estate in Pearl street, a large house and grounds, for the use and benefit of the blind, provided that the city of Boston would raise $50,000 for the same purpose."

Howe was no dreamer. He was a man of affairs; a sane humanitarian; a tempered enthusiast. New working machinery was necessary; he created it, instructing his assistants so thoroughly that later, when the Sydenham school was established in England, a corps of Howe's former pupils were secured as teachers. He invented a novel form of raised letters for the books of the blind; and the first product of his press was a Bible which was published in 1843—a book half the size, and produced at half the cost, of that Scriptures for the Blind then recently brought out in England.

As a school-master of the blind, Howe was prolific of new and shrewd ideas for the discipline of children. The old Adam enters into these youngsters as well as into their more fortunate fellows whose vision is unclouded. Howe used to maintain that punishments and rewards are mere conventions. Stand a boy on a stool, with a paper-cap on his head; tell him that he is good and happy there and to be envied, and watch him preen himself like a young peacock. Give him a box of caramels, marked medicine, and see him groan and weep as he chokes them down. So Howe inspired his pupils with a sense of receiving merit-marks when they went to bed early, took cold baths, ate a wholesome diet, and exercised daily in the open air.

With this work for the blind securely launched, Howe found himself a mature man of many cares and experiences, approaching middle age. He was untiring. To test upon himself the continued sense of total darkness he blindfolded himself, and so went about for weeks. He learned to use the blind boys' types as skillfully as his best pupil; and with his eyes darkened he might be seen wandering about the streets in tow of a dog on a string. By such means he came to have an intimate appreciation of the atmosphere, the sensations, and the limitations of the blind, their capacities and their possible ambitions. Truly it was a care of the blind leading the blind; but ditches were friendly in those days, and walking was on the level.

Those were indeed times when light was beginning to shine in dark places. The great wave of modern altruism was rising. New ideas of expanding helpfulness were awaking civ-

ilized minds. In France and Germany even honest men were seeing visions, while in Great Britain and America such popular prophets as Charles Dickens were lashing abuses, breaking down intrenched officialdom and rending consecrated cruelty. It was that era of political liberalism which culminated in the English Reform Bill, the Continental Revolution of '48, the freeing of Italy, the Emancipation of Russian Serfs, and the American Civil War; while behind these great movements there advanced haltingly, at times timidly, often mistakenly, as Brook Farm could testify—but always surely, that deeper, more wide-reaching wave of social liberalism, which was beginning to teach men that a drunkard is not a noble fellow; that a bully is not a hero; that poverty is not a crime; that weakness is not contemptible; that labor is not disgraceful; that misfortune is not misconduct; that the maimed, the halt, and the blind should not expiate the sins of their fathers; that the love of nature, of little children and of dumb creatures is not ignoble, and that the uplift of man is an undertaking worthy the best culture, the perfect science and the life-long effort of the finest minds. Such conceptions of a better humanity were in the making when Samuel Howe was in his prime.

Himself a leader of the silent revolution, he moved on from task to task; his clear intellect discovering new points of attack, his genius lighting the pathway to achievement.

In the last analysis the object of all human endeavor is human happiness. Howe was one of those rare men to whom this truth is a present fact. He saw that happiness for the individual is in direct relation to the temperament, the experience and the purposes of the individual. He aimed at relieving misery on a great scale, at raising to a higher level whole groups of men; but sanely, he saw that cakes and ale suffice for most of us. Caviar and champagne are not necessary for humble souls. Nonsense-hubbub did not spur him to the impossible; nor the groans of cynics turn him aside from the work in hand. He was a prophet of fairplay.

One conceives with difficulty the intellectual limitations of a person deprived of nearly all senses except the sense of touch. The state of a blind man is sad enough, but Howe's most famous pupil had neither sight, hearing, taste, nor smell. The training of such an unfortunate to a perception of the good things of life—to an appreciation of literature, music, and art is incredible at first thought, but Howe succeeded in this astonishing task. His subject was Laura Bridgman, the famous blind deaf-mute, whom he found at Hanover, New Hampshire, brought to Boston, when she was a child of eight, and educated at the Perkins Institute. Dickens describes the girl. That great man had a constant curiosity about and interest in schools, asylums, and prisons, making them the first object of his visits to new places. His delighted appreciation of the story of Laura Bridgman appears in a charming sketch.

For 43 years Howe was superintendent of the Perkins Institute. That work is his monument; but like other busy men he found time for other things. He became interested in the state of deaf-mutes, and in season and out, he preached his convictions. Especially the feeble-minded among such children claimed his regard. He asked permission of the Asylum at Hartford to test his convictions there, but was refused. Then he undertook experiments of his own. With two feeble-minded deaf-mute children as pupils in their own homes, he began quietly a system of simple instruction; teaching them easy and familiar arts by constant repetition and practice, until the doing of their tasks became to them automatic. Quickly parents were interested and then enthusiastic. The interest of the children themselves was stimulated, and their feeble intelligence aroused. The investigation was soon placed beyond the experimental stage. Howe demonstrated that the children need not grow up helpless dependents, but in some fashion might become humble bread-winners; then he presented his scheme to the authorities of the Commonwealth. The authorities approved; the legislature took action, and the small beginning developed into that useful institution, the Massachusetts School for Feeble-Minded Children.

One regrets that Howe had passed his prime when the Civil War came. I believe that at his best he would have been a great figure in that struggle. The double interests, emancipation, and union, were certain to appeal strongly to a man of his training and sympathies. He became actively engaged in the anti-slavery movement as early as 1851, and for several years was an editor of the "Commonwealth," a journal of that cause. During the war he was employed as a member of the Sanitary Commission, and was busily concerned in establishing the Freedman's Bureau. It was all good, serviceable inconspicuous work. He had then reached the age when an active man, with his reputation made, is in demand for everything from an after-dinner speech to the presidency of an insurance company, and Howe was unable to escape such burdens. In 1865 he was made chairman of the Massachusetts State Board of Charities, in which position he proved an untiring reformer, to the amazement of his breathless associates. His "General Principles of Public Charity" was a textbook, and is a classic still in demand.

In 1869 Howe had an experience which took him back to the scenes of his youthful crusade of forty years before. The Cretan insurrection of '66 was becoming an international problem. Greece was taking sides with Crete against Turkey, and the powers were bestirring themselves in the matter. But Howe was bestirring himself also. While cabinets were settling the status of the unhappy island, and handing it back to the gentle leading of Turks, Howe was organizing a relief expedition to feed and clothe the destitute people. He followed his plan of 1828; raised a large sum of money, loaded a ship with supplies, and visited Crete. His work there was delicate and hazardous, but he completed it, and saved thousands from starvation. Then he visited the Greek mainland, and learned to his delight that he was not forgotten there. The visit was a triumphal progress, for he found himself one of the immortals among those warm-hearted people. At threescore-and-ten the freedom of cities is pleasant, and laurel still becomes the ancient brow.

That was Howe's last happily successful endeavor. He returned with added honors to America, and promptly was

called to further public work. The federal congress was bestirring itself in the early throes of imperialistic ambition, and folk talked seriously of annexing the islands of the sea. Santo Domingo was their first object, and thither went Howe with other forlorn commissioners, by direction of President Grant. It was a situation of curious paradox,—the Apostle of Freedom, the Hero of Greece, and the Champion of Slaves, sailing away on a mission to annex the parti-colored rabble of a farcical Carib republic. The object was a failure, as we know.

Howe came home, but went back later to the island, seeking health and forwarding a commercial enterprise. This expedition was a double failure, and our philosopher returned to Boston a broken man. His end was near. Much buffeting and novel strivings do not conduce to a peaceful old age. He died with little more ado, in his 75th year, on the 9th of January, 1876.

We have seen that here was a man of singular abilities, of noble aims, of quaint simplicity, of perfect courage. Among the great physicians of America his career is one of the most romantic and varied, and his accomplishments lasting. It is a name to be guarded in our annals, for he wrought and suffered much. In his native town they paid him public honors, and great ones of the earth told what he had done.

Here are the final charming words of Howe's old friend, the poet-statesman Hoar: "His is one of the great figures in American history; I do not think of another who combines the character of a great reformer, of a great moral champion, of a great administrator of great enterprises, requiring business sagacity and wisdom as well as courage, always in the van, with the character also of a knight-errant who crossed the sea, like the Red Cross knight of old, to champion the cause of liberty in a distant nation. There was never on the soil of America, fertile as that soil has been of patriots and heroes and lovers, a more patriotic hero, a more loving knight."

AN ADENOMA OF ISLAND OF LANGERHANS.

By Henry F. Helmholz, M. D.,

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The rarity of benign tumors of the pancreas and the interest as to their histogenesis makes it seem of sufficient value to report this case, which is otherwise of no great interest. The origin of epithelial tumors of the pancreas may be threefold: (1) from the duct epithelium, (2) from the pancreatic cells proper, and (3) from the cells of the Langerhans islands. Tumors arising from the first two of these sources have been repeatedly described, but growths originating in the islands of Langerhans are rarer in literature. In 1902 Fabozzi[1] reported five cases of carcinoma of the pancreas, all of which he describes as arising from the islands of Langerhans. Reitman[2] in an article published in 1905 is very emphatic in his objections to the work of Fabozzi, insisting that he had to do with sclerosis of the pancreas in which the approximation of the islands resembled carcinomatous acini. The figures given by Fabozzi are unsatisfactory in that they show only single acini of the tumors. In 1902 Nichols[3] described an adenoma of the pancreas which he thinks took origin in the cells of an island of Langerhans. His photographs and descriptions tally very closely with the adenoma to be described in this paper.

The tumor which measured only 5 mm. in diameter, was discovered by chance when examining the routine block of tissue removed for microscopical study. It was found in the pancreas of autopsy 2364, of the Johns Hopkins Hospital pathological series. The abbreviated protocol is as follows:

H. B., male, aged 65 years. Ward M. 1904.

Anatomical diagnosis.—Arterio-sclerosis; cardiac hypertrophy and dilatation; bilateral hydro-thorax; atelectasis of right lower lobe; chronic passive congestion of lungs; chronic fibrous pleuritis; chronic passive congestion of liver and spleen; chronic diffuse nephritis.

Body is that of a well-nourished negro, 161 cms. in length. The left pleural cavity contains 1600 cc. of clear yellow fluid, the right about one-half that amount.

Heart weighs 500 gms. The right and left ventricles are slightly dilated and hypertrophied, their walls measure 6 and 16 cm., respectively, in thickness.

Lungs are deeply pigmented and in section are of a salmon pink color. The right lower lobe is of dark red color, atelectatic and of leathery consistency.

Spleen measures 11 x 6.5 x 3.5 cms. and weighs 100 gms. The organ is very firm and its capsule thickened. On section the trabeculæ stand out prominently in the purplish red pulp, and the malpighian corpuscles are just visible.

Liver measures 26 x 19 x 6.5 cms. and weighs 1450 gms. On section is shows the typical nutmeg appearance.

Kidneys.—The left kidney measures 9 x 5 x 2.5 cms. and weighs 100 gms. The capsule strips off quite readily, but carries with it numerous small particles of the cortex. The surface is granular and mottled reddish brown and yellow. On section the cortex measures 5 mm. across. The striations are fairly regular. The right kidney measures 10 x 5 x 2.5 cms. and weighs 120 gms. It resembles the left.

Bladder.—On opening the bladder two small angular stones were found lying on a normal cystic mucous membrane.

Pancreas.—On section appears normal.

Stomach and *Intestine* also appear normal.

[1] Fabozzi: Beiträge zur Path. Anat. u. z. allg. Path., Vol. XXXIV, p. 1, 1902.

[2] Reitman: Zeitschrift f. Heilkunde, Vol. XXVI, p. 1; N. Folge, Vol. VI., 1905.

[3] Nichols: Jr. of Med. Research, Vol. III, p. 385, 1902.

Aorta has on its surface numerous atheromatous plaques and ulcers.

The section were stained with hæmatoxylin and eosin, polychrome methylene blue, Mallory's connective tissue stain and phosphotungstic hæmatoxylin.

Microscopical Notes.

The pancreas shows a slight increase in fibrous tissue that is not uniform in distribution, but is marked in certain of the lobes and practically absent in others. The parenchyma cells appear normal, as do those of the islands of Langerhans. In some of the islands the structure is somewhat disturbed on account of postmortem change.

The tumor nodule measured 5 x 3 x 5 mm. It was not visible on the surface, and only on section could it be seen as a dull gray, finely granular area sharply circumscribed on all sides by a thin capsule. The adjoining pancreatic tissue is somewhat compressed, and in it there are several islands of Langerhans which are flattened out. Toward one side where the tumor forms the periphery of a pancreatic lobule, the capsule is well defined, but toward the lobular parenchyma it is made up of only a few strands of fibrous tissue. Its surface is everywhere smooth, except at one point, which is shown at *A* in Fig. 1, where the tumor seems to have grown beyond its capsule. With the connective tissue stain a few fine connective tissue fibers can, however, be demonstrated encapsulating it at that point. The tumor itself has a stroma of connective tissue carrying blood vessels, which is rather delicate and which forms large meshes. In these spaces there lie solid or hollowed out, anastomosing masses of epithelial cells, which are quite widely separated from the stroma, evidently by retraction. They are sometimes many cells wide, without a break in their continuity. In places blood vessels may be seen running through the cell masses, and lying in little spaces among the cells. In other places there are definite lumina about which epithelial cells are radially arranged, and about which they seem more columnar in form than elsewhere. At one point just within the capsule several duct-like acini lie embedded in a band of fibrous tissue as it passes inward from the capsule. The alveoli are lined by a single layer of cuboidal epithelium. Its protoplasm is clear and stains very lightly with eosin, its nuclei stain a very pale blue and contain no chromatin network. Embedded as they are in connective tissue, and not found in any other part of the tumor they undoubtedly represent duct acini that have become surrounded by the advancing tumor edge. The alveoli contain granular coagulated material, together with cells of various kinds, some of which are nucleated wandering cells, while others are red corpuscles. The vascular supply shows nothing of interest.

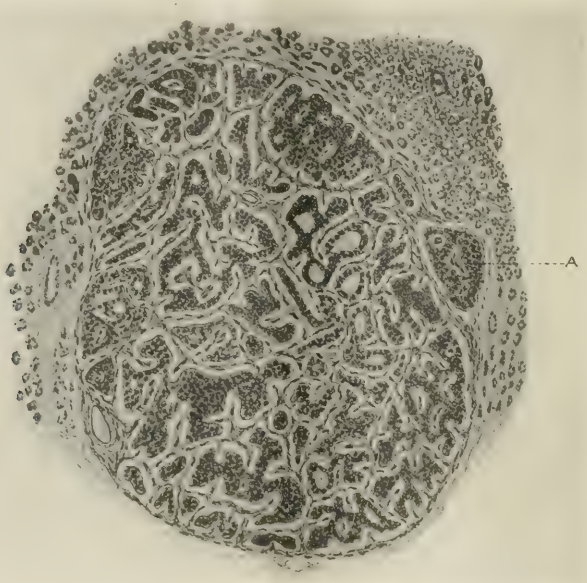

Fig. 1.

Examined under the high power (Zeiss obj. DD. Ocular 4), the cells are in general very indistinctly outlined, rather polyhedral in form, and slightly larger than those of the pancreatic parenchyma. Their protoplasm is coarsely granular, and takes a faint pink stain, in contrast to the basophilic pancreatic cells. About the lumina which have been above described the columnar cells take a redder stain. The nucleus in these cells is situated as far as possible away from the

lumen, the cell margin is quite refractile and sharp, and in places there is an appearance almost as if there was a ciliated margin. The nuclei contain a well defined chromatin network, in which are seen from three to five chromatin bodies. On looking carefully through ten sections of the tumor no mitotic figures were found. The stroma is quite cellular and so finely divided that sometimes a single connective tissue cell is seen lying in the epithelial masses. In the stroma wandering cells are fairly numerous. The pancreatic cells in the capsule are shrunken and atrophic, containing small, irregular, uniformly staining nuclei.

The case reported by Nichols and the one by Reitman are given below. For the other cases the reader is referred to Nichols' article.

Nichols' case.—"Simple adenoma of pancreas." The tumor was found accidentally at autopsy. It consisted of a flattened nodule, of tawny yellow color with a few distended blood vessels over its surface. On section it was definitely circumscribed, rather soft and on pressure exuded a small amount of blood. The tumor was the size of a marrow fat pea. The capsule was regular and at no point infiltrated. Large cell masses bounded by anastomosing bands of connective tissue gave the tumor an alveolar structure. The cells resembled the pancreatic cells, and were columnar or polyhedral depending on the arrangement about the alveoli. The protoplasm was eosinphilic and granular, the nuclei large, round and vesicular. The author regards the island origin of the tumor most probable.

Reitman's case.—"In association with purulent pancreatitis was seen a peculiar adenomatous structure greatly resembling the islands of Langerhans." The tumors were found in a man 62 years of age. The microscopical examination of the pancreas showed a marked inflammation limited to the ducts. Normal islands were present in large numbers. In the head of the pancreas taking up as much as a single lobe were found structures that resembled the islands of Langerhans in their method of construction and in their mode of growth, but in the histological characters of the cells resembled more a tumor arising from the ducts. No relation could be demonstrated to the ducts, however. The cylindrical cells contained no giant nuclei or mitotic figures. The tumor did not show the vascular supply of the islands. The author leans toward the duct origin of the tumor. The drawing the author gives of the tumor shows it to differ considerably from the one described in this article.

In attempting to establish the origin of this adenoma the following facts, briefly summed up, tend to show that in all probability the tumor arose from the cells of the islands of Langerhans:

(1) The anastomosing arrangement of the acini: The structure of individual lobules of the tumor if displaced into normal pancreatic tissue would be indistinguishable from islands of Langerhans.

(2) The intimate relation of the capillaries to the epithelium in some parts of the tumor.

(3) The characteristics of the tumor cell: The polyhedral form of the cell; the acidophile staining of the protoplasm; the varying size of the nucleus; its vesicular character and its numerous large chromatin bodies are characters which the tumor's cells and those of the islands of Langerhans have in common.

NOTES ON NEW BOOKS.

American Text-Book of Surgery for Practitioners and Students. By eleven American authors. Edited by WM. W. KEEN, M. D., LL.D., F. R. C. S. (Hon.), and J. WM. WHITE, M. D., Ph.D. Fourth edition, revised and enlarged. *(Philadelphia, New York, and London: W. B. Saunders & Co.)*

This text-book on surgery is too well known in this country to need any special introduction. That it has proved a useful book to many is indicated by the fact that new editions have been called for at frequent intervals since the publication of the first edition. Any one volume text-book on surgery is certain to be more or less unsatisfactory, in most cases, for the reason that there is so large a field to cover, and text-books written by a large number of different authors are certain to vary in the excellence of their chapters. A chapter that is very satisfactory in this book, is that devoted to the surgical diseases and injuries of the head. Probably no short discussion of this subject can be found which is as entirely satisfactory. The chapter on genito-urinary surgery is also good but it occupies a disproportionally large amount of space. In this particular, the book is far from well balanced throughout. For example, much less space is devoted to the discussion of ether anesthesia than to the technic of the operation of rhinoplasty. Over sixteen pages are devoted to the various methods of treatment alone of stone in the bladder, two pages more than is devoted to the entire subject of appendicitis. We are surprised to see many antiquated, and in some cases, discredited operations given a good deal of space. For example, nearly three pages are devoted to castration and vasectomy for prostatic enlargement; procedures which have been given up as of little value by most modern surgeons and which, the writer admits are still only on trial. The discussion of the very fundamental subject of hand disinfection decidedly lacks the thoroughness which is characteristic of the best American operating rooms. We are sorry to see Fürbringer's method given, in spite of the fact that laboratory and clinical evidence has shown it to be unreliable. From the high death rate which has been shown from the experience of many surgeons, spinal anesthesia does not seem to deserve more than mention, at least not without caution as to its dangers and relatively high mortality as compared with ether and chloroform. The directions for the use of local anesthesia are most imperfect and if followed as given in the book, the anesthesia is certain to be found unsatisfactory. From the title of the book one would expect to see the work of American surgeons receive prominent mention. It is surprising that not only is such mention frequently neglected, but less desirable methods are given in place of American methods. For instance, we are surprised to see that the Connell method of intestinal anastomosis is not given a place among the numerous other methods described and depicted, although

a large number of American surgeons consider it the best method that has yet been devised. Ochsner's method of treating appendicitis is not mentioned, neither are the fundamental studies of Opie in connection with pancreatitis. Finney's pyloroplasty, a favorite method in America, is given two lines, while the procedure of Heineke and Mikulicz, which is now practically never used, is given three illustrations and a page of print. In orthopedic surgery, we miss any mention of the use of the Taylor back brace, the Bradford frame, the Boston Children's Hospital method of applying Plaster of Paris casts for tuberculosis of the spine; Goldthwait's studies on joint affections; and Sampson's thorough work in connection with flat foot. Numerous other instances might be mentioned if space permitted of the lack of recognition of American work in this American text-book. In these days when every medical student is expected to have a special course in gynecology and practically always owns a text-book on this subject, it seems unnecessary to devote valuable space to a very imperfect treatment of the subject, when the space is so much needed for the more thorough discussion of general surgery. The same is true of surgical bacteriology, in which subject, every well-equipped medical school gives a thorough laboratory course. Considerable unnecessary space is also taken up with procedures which are now practically never used and are generally considered out of date. Among these may be mentioned, blood letting, cupping, scarification, and blistering. In too many cases the book is a indiscriminate compilation. Many methods are given with no advice to help the student or practitioner to select the one best adapted to the needs of the special case. Many of these criticisms would apply to several other text-books on surgery which have appeared in recent years. We have already mentioned several admirable features of the work which will commend it to many surgeons and practitioners, and the large number of teachers associated in preparing the book will insure the usual large sale among students.

The Practice of Obstetrics. Edited by REUBEN PETERSON, A. B., M. D. *(Philadelphia and New York: Lea Brothers & Co., 1907.)*

This book is edited by Peterson, but the various chapters are written by several well-known men.

Some chapters are good but as a whole the book is no improvement over the many works on Obstetrics written in recent years; in fact it is not as good as most of them, and therefore we can hardly see the use in publishing it.

Plaster of Paris and How to Use It. By MATIN W. WARE, M. D., Adjunct Attending Surgeon, Mount Sinai Hospital, etc. *(New York: Surgery Publishing Company, 1906.)*

This is an excellent little volume, well arranged and illustrated. Its object is to teach medical students how to make plaster bandages and how to apply them to all the more common needs. From its simplicity and compactness, as well as clearness of exposition its success would seem to be assured, as, so far as the reviewer knows, there is no other book of this size which covers the subject so satisfactorily. R. N.

A Text-Book of Physiology for Medical Students and Physicians. By WILLIAM H. HOWELL, Ph. D., M. D., LL. D., Professor of Physiology in the Johns Hopkins University, Baltimore. Illustrated. *(Philadelphia and London: W. B. Saunders & Co., 1905.)*

The number of text-books of physiology written for medical students and practitioners that each year sees the light of day is no smaller than it is in the case of text-books of other subjects of medical interest. Most of such books are written in a stereotyped fashion, which usually is determined by some successful text-book writer of a decade or two or three ago. Every now and then, however, a work appears which is quite distinctive, it may be, in more ways than one. The book before us fits into this category. A few quotations from the author's preface will serve to indicate some of the qualities which seem to make it distinctive as well as to point out to the reader the author's guiding principles in the preparation of the book. "Simplicity and lucidity in the presentation of facts and theories" seems to have been the author's first aim. That he has succeeded in making a high record may be taken for granted, at least, by those who have already had the opportunity of enjoying other productions of this author's pen.

A second point the author has borne in mind in the preparation of the book is "the need of a judicious limitation of the material selected." "Every specialist is aware of the bewildering number of researches that have been and are being published in physiology and the closely related sciences, and the difficulty of justly estimating the value of the conflicting results." For beginners it is necessary to bring "within reasonable limits" both the amount of material as well as the discussion of details of controversies. "The author must assume the responsibility of sifting the evidence and emphasizing those conclusions that seem to be most justified by experiment and observation. As far as material is concerned, it is evident that the selection of what to give and what to omit is a matter of judgment and experience on the part of the writer, but the present author is convinced that the necessary reduction in material should be made by a process of elimination rather than by condensation." For the purposes of the student "brief, comprehensive statements are oftentimes misleading, or fail at least to make a clear impression. Those subjects that are presented to him must be given with a certain degree of fullness if he is expected to obtain a serviceable conception of the facts." "The obstacle that is most frequently encountered by the student lies in the complexity of the subject—the large number of more or less disconnected facts and theories which must be considered in a discussion of the structure, physics, and chemistry of such an intricate organism as the human body. But once a selection has been made of the facts and principles which it is most desirable that the student should know, there is no intrinsic difficulty to prevent them from being stated so clearly that they may be comprehended by anyone who possesses an elementary knowledge of anatomy, physics, and chemistry. It is doubtless the art of presentation that makes a text-book successful or unsuccessful."

These, then, are the difficulties which the author believed he had to overcome in the production of a successful text-book. The proof as to whether or not the effort was, or, rather, is a successful one, will be the extent to which the work is adopted by classes of physiology. The reviewer's view is expressed in the opinion that the work will come to be the standard text-book in medical schools throughout the English speaking world.

The author's words quoted above will serve to indicate better than the reviewer could state it the style of the book in general.

The arrangement of material also differs from that now in general vogue in that the physiology of the nervous system and that of the special senses follow immediately upon the section, the first, on the physiology of muscle and nerve. Other sections are blood and lymph, the physiology of the organs of circulation of the blood and lymph, the physiology of respiration, the physiology of digestion and secretion, nutrition and heat production and regulation, and the physiology of reproduction. Since the work contains no chapter on the physiology of the cell it is evident that it is the author's opinion that this is a subject which should be eliminated in the process of reduction of material to be presented to the student.

The book abounds in judiciously selected illustrations, many of

which are original. Many references to the literature have been given and "these have been selected usually with the idea of citing those works which themselves contain a more or less extensive discussion and literature." Upon glancing over the footnotes one is struck by the frequency with which the name "Johns Hopkins" appears. The reviewer is unable to decide whether this is to be accounted for by association or by the part this institution has played in the upbuilding of physiology in this country.

Progressive Medicine, Vol. I, March, 1907. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M. D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia. Octavo, 280 pages, with illustrations. *(Lea Brothers & Co., Publishers, Philadelphia and New York.)*

The subjects dealt with in this volume are: Surgery of the Head, Neck, and Thorax, by Dr. Charles H. Frazier; Infectious Diseases, including Acute Rheumatism and Croupous Pneumonia, by Dr. Robert B. Preble; the Diseases of Children, by Dr. Floyd M. Crandall; Rhinology and Laryngology, by Dr. D. Braden Kyle; and Otology, by Dr. B. Alexander Randall. The reviews are carefully prepared, and the most important articles that have appeared during the past year under these various titles fully abstracted. The volume is thus useful largely as one of reference, as with its index it furnishes an easy means to find out what has been written on a given topic within twelve months.

R. N.

A Text-Book of Ophthalmic Operations, by H. GRIMSDALE, M. B., F. R. C. S., and C. BREWERTON, F. R. C. S. *(Chicago: W. T. Keener & Co., 1907.)*

The title of this book is Text-Book of Ophthalmic Operations and, if the purpose is to familiarize the reader with the names of various men who have modified accepted operative procedures in more or less minor ways, it will serve its purpose. We assume, however, that it is the intention of the authors to produce a text-book which would describe in sufficient detail and with clearness operative procedures generally adopted at the present day, and if this was their intention, they have surely failed.

The book shows no evidence of originality. The various operative procedures are described oftentimes with the lack of the detail and precision which would insure success, and there is an absence of suggestions as to the choice of operations, and no attention is paid to the consideration of the various problems of operative diagnosis, *i. e.*, cases suitable for operation, time for operation, etc. Operative preliminaries which play such an important role in eye work, *i. e.*, means of rendering the conjunctival sack as free as possible of bacteria, the use of cocain preparatory to cataract extraction, the importance of using atropin before doing a discission are subjects which are not mentioned in its pages, although they are extremely important. For instance, before describing the operation of discission, the authors merely say, "For soft lenses, the method of election is by discission." Here we find no mention made as to what constitutes a soft lens, nor the importance of using atropin eye drops before and after the operation without the use of which the operation might be ruinous.

Many of the descriptions of the operations are so incomplete as to be useless; for instance, the operative treatment of chalazion is dismissed with the statement "Oftentimes it is enough to incise them from the conjunctival surface and evacuate their contents." The reader who wishes to know how to do is no wiser from having read this. Again in the treatment of lachrymal affections no mention is made of the means of passing the probes, the difficulties met with, etc., which a reader of a book of this title has a right to expect. While the operation for cataract is described in some detail, no mention is made of the after-treatment of the case—as to the use of atropin, bandaging one or both eyes and for how long, details which worry the operator more than the operation itself, and upon which the success depends so much.

In conclusion, we must say that while the authors have gone out of their way to describe various operations which are of no value, *i. e.*, Hanock's operation, Querenghi's, Heine's, Hern's, etc., they have not described the important and recognized standard operations with the clearness, fullness, and exactness which one must demand from a book of this character. We consider this book of no value to the advanced worker and of no value to the inexperienced one, who would soon get into disaster if he had no other help than that derived from this work.

The lack of precision, care or "finesse" so evident in the preparation of the text is likewise shown in the illustrations, which, while only schematic, are very crude and "clumsy" and have no tendency to impress one with the delicacy of the operative manipulations on or about the eye.

B. B. B., JR.

The Integrative Action of the Nervous System. By Charles S. SHERRINGTON. *(New York: Charles Scribner's Sons, 1906.)*

Epitome.—The parts of the work which readily admit of being summarized are the following:

The nervous system unites separate organs in such a manner that there results "an animal possessing solidarity, an individual." This is its "integrative action." . . . Since every path and part of the nervous system is connected with every other path and part more or less directly, it follows that a stimulus applied anywhere can affect the whole system to a greater or less extent, and that a truly *simple reflex* cannot exist. Nevertheless the simple reflex is a very convenient abstraction and may be regarded as the ideal unit of nervous action. The characteristics of simple reflex conduction will be considered first, and subsequently the coordination of reflexes will be discussed. . . . . Every reflex action is separable into three processes and every reflex arc into three parts corresponding to the processes in question. These parts may be called the *receptor*, *conductor*, and *effector* organs. The reflexes which form the basis of the discussion are those which have been carefully studied by the author in the spinal mammal, namely, the flexion reflex, the scratch reflex, the extension thrust and the crossed extension reflex. There are also frequent references to the work of others on other groups of animals invertebrate as well as vertebrate. . . . . Reflex conduction differs from nerve trunk conduction in several particulars, *e. g.*, in the former the time elapsing between the stimulation and the response is longer, the after effect is prolonged, the direction of conduction is irreversible and so forth. A study of these peculiarities of reflex conduction leads to the conclusion that there is interpolated into the reflex path a region (*synapse*) between axon and dendron which has different properties from the rest of the nervous arc. The phenomenon of Wallerian degeneration supports this view which may also be expressed by saying that there exists some sort of interneuronic plane of separation. . . . Reciprocal inhibition or the inhibition of muscles antagonistic to those excited is a frequent phenomenon in reflex action. Since inhibition can be obtained by stimulating the lateral cephalad end of the divided cord, it is evident that the inhibitory process does not occur in the receptor or first afferent neuron but must take place somewhere nearer to the motor end of the reflex arc. The very great importance of inhibition as a factor in coordination of reflexes can be realized by comparing the normal animal with one which has been poisoned

by strychnia or tetanus toxin. These substances can be shown to convert the normal inhibitory process into excitation with the result that coordination is completely lost. . . . A given receptor transmits only those stimuli which are applied to the one small area which it supplies, and therefore is in a sense a *private path*. On the other hand, all reflexes which act upon the same motor mechanism travel over paths which must converge upon the effector which thus becomes the *common path* of all these reflexes. The essential feature in the coordination of reflexes is the adjustment which prevents the interference or conflict of reflexes which employ the same common path. . . . Reflexes which employ the same common path in the same way, that is, which either excite or inhibit the end organ, reinforce each other so that a response may occur even when all the stimuli are subliminal. These are *allied reflexes*. Reflexes which employ the same common path in different ways, that is one excites while the other inhibits, are *antagonistic reflexes*. The result is not the algebraic sum of the results obtained when both occur separately. One of the reflexes becomes for the time *prepotent* while the other drops out entirely. . . . While the occurrence of a reflex favors the simultaneous production of allied reflexes, it also favors the subsequent production of antagonistic reflexes. For example, flexion facilitates subsequent extension and this a still more subsequent flexion and so on. The advantage of such an arrangement in such reflexes as walking, scratching, and so forth, is obvious. . . . Reflexes which are *extro-ceptive* in character, *i. e.*, due to external stimuli applied to the skin, may be reinforced by proprio-ceptive reflexes (*i. e.*, due to gravity and mechanical stimuli arising in the muscles, joints, and so forth.) Thus when the stimulation of the skin of the foot causes a flexion reflex, this reflex is reinforced and prolonged by reflexes arising in the muscles and joints during the act of contraction and having the same final common path as the extro-ceptive reflex. . . . If the strength of a stimulus is gradually increased the effect spreads involving a greater and greater number of reflexes in the response until a certain limit is reached. In the case of the flexion reflex a minimal stimulus causes a contraction of part of the hamstring muscles only, but on increasing the strength of the stimulus the response becomes more and more widespread until it involves the four limbs, neck, head, and tail. Certain reflexes, however, as the pinna reflex, cannot be elicited no matter how strong the stimulus to the foot. . . . It is usually stated that the nerve impulse travels over one arc rather than another because the various arcs offer different amounts of resistance. It is possible to speak a little more definitely. In order to produce a response the impulse which reaches a synapse must be more than a subminimal stimulus for the next neuron. The neurons differ in excitability and in any one neuron the different dendrites might differ in their excitability. To this the different resistances of the paths is partly attributable. The total resistance of an arc depends partly upon the number of neurons involved and partly upon the threshold of the least excitable neuron. . . . The final common path is used in only one way at a time. Of two contending reflexes one only is prepotent and takes possession of the final common path. The prepotence of a reflex depends upon four factors. These are (1) facilitation—the presence of allied reflexes causes simultaneous lowering of the threshold for the stimulus calling forth the reflex in question or the presence of antagonistic reflexes causes as an after effect a similar lowering of the threshold; (2) fatigue—if after stimulation of one point until fatigue appears a neighboring point be stimulated, the reflex begins again with its original vigor. As the reflexes from the two points have the greater part of their arcs in common, the region where the fatigue occurs must lie near the sensory end of the arc, possibly at the first synapse; (3) intensity of the stimulation; (4) the species of reflex—the noci-ceptive reflexes are those which tend to protect the animal from harmful stimulation, *e. g.*, flexion of the leg on stimulation of the foot. These reflexes are the most potent while those tonic reflexes which are of use in maintaining posture and so forth are the weakest. . . . From the point of view that reflexes are adaptations it is not unscientific to seek for the purpose or end of the various reflexes. In the flexion reflex one sees a protective withdrawal of the hind leg, the extensor thrust is a galloping movement and so forth. . . . *Spinal shock* is a depression or suppression of the nervous functions which is the immediate result of severe injuries of the nervous system. It is most marked in man and the anthropoids. The reflexes are affected in varying degrees, the noci-ceptive least of all. The condition seems to be due to the cutting off of impulses from the mid-brain and pons which originate in the eye and otic labyrinth. . . . Just as we speak of the local sign of a conscious sensation so we may speak of the local sign of a reflex. For example, the foot engaged in the scratch reflex becomes directed to a different spot if the point of stimulation is changed. . . . With the noci-ceptive reflexes are associated certain subordinate movements, for example, growling, snapping, showing the teeth, and so forth. This makes it probable that in the normal animal the noci-ceptive reflexes are accompanied by those cortical processes which are causally connected with the sensation of pain. It is probable, therefore, that the fibers which function in these reflexes are the pain fibers. The noci-ceptive fibers pass up the cord in the ventral part of the lateral column chiefly of the opposite side. . . . Several psychologists have regarded the emotions as due to the perception of altered conditions of the viscera. This view is disposed of by the fact that when the cord and both vagi have been cut, the animal shows no lack of emotion, but may be pleased or angry as before.[1] . . . The relation of the functional areas of the brain to the cerebral convolutions is very inconstant. In surgical operations it is best to test the cortex by electrical stimulation and not to trust to anatomical landmarks. Beevor and Horsley were correct in their statement that the motor cortex occupies a relatively smaller area in the anthropoids than in the lower monkeys. . . . In the movements which are produced by cortical stimulation the inhibition of antagonistic muscles is observed. . . . Under normal conditions certain movements are never obtained by cortical stimulation, for example, closure of the jaw. These movements can be obtained after poisoning with strychnia and tetanus toxin and it is therefore probable that the cortex normally has an inhibitory action on the muscles in question. . . . In *decerebrate rigidity* the contracted muscles are those which are normally unaffected by stimulation of the cortex. The cutting off of the higher centers allows the normal reflex tone of these muscles to become greatly increased. The reflexes are proprio-ceptive and originate in the muscles, joints, and so forth, but especially in the vestibule. It is possible to divide the whole musculature into two parts, the *tonic* and the *phasic*. While the former is called into action in the proprio-ceptive reflexes and is inhibited by the cortex, the latter is extro-ceptive in character and may be called into action by stimulation of the cortex. The former acts constantly and have for its end the maintenance of posture and equilibrium, the latter act intermittently and

[1] The value of this experiment is questionable. The author's dog barked and so forth, and from this we may justly infer that the animal was angry. But we cannot say that the dog would not have felt more angry could its emotions have been accompanied by movements of the legs and changes in the viscera. Indeed we can know nothing about it until we study subjectively the effect upon our emotions of non-irritative section of all the efferent fibers.

are employed in special movements. . . . The consideration of the nervous system as a whole presents great difficulty. It may perhaps help us to understand the cause of the predominence of the brain. If we examine the nervous systems of various animals beginning with the simplest, it is seen that the first step is the development of a summating and coordinating mechanism, the central nervous system. The central nervous system unites not only the organs present in each metamere but also like organs in different metameres. Certain segments develop special receptors. Those of smell, sight, and hearing (distance receptors) have vastly greater possibilities of exercise and usefulness than the local receptors, touch, and so forth. The proprio-ceptive reflexes increase in importance from their associated action with the distance receptors. The most important proprio-ceptors are those arising in the vestibule and semi-circular canals. Thus it happens that in the brain are found the principal extro-ceptive and proprio-ceptive centers. The cerebrum is the ganglion of the extro-ceptive distance receptors, while the cerebellum is that of the proprio-ceptive. This preponderence of the brain over the rest of the central nervous system is the chief factor in the integration of the individual. . . . By an appropriate apparatus spots of light which flicker more or less may be cast upon either or both retinas at will. Experiment showed that the right and left eye images were still distinct when they reached that region of the brain which is associated with consciousness. . . . The attempt to separate psychology and physiology is to be deplored. Much light may be thrown upon the integrative action of the nervous system by the joint working of these sciences.

Criticism.—In its phraseology this work is terse, often elliptical, its transitions are abrupt, its digressions confusing, its subheadings often ill-chosen and the arrangement of the material generally bad. It is usually possible to find out what the author means but this frequently involves a great expenditure of time and energy. In these respects the book is considerably worse than the majority of English and German scientific writings. Apart from the style the work is of unusual merit. The author seems always to look beyond the simple facts and to complete them with his rich but sane imagination, and although his attitude is markedly philosophical it is none the less wholesome and scientific on that account. PERCY M. DAWSON.

Transactions of the American Gynæcological Society, Vol. XXXI. (Philadelphia: Wm. J. Dornan, Printer, 1906.)

As an exposition of the present status of gynæcology in the United States, and of the views of the leading surgeons in this specialty, these transactions are most important, and, therefore, the volume requires no further recommendation to the profession. R. N.

Essentials of Medical Electricity. By EDWARD REGINALD MORTON, M. D., pp. 175 +, XI, with 11 plates and 70 illustrations. *(London: Henry Kimpton. Chicago: W. T. Keener & Co., 1906.)*

Over half the book is a synopsis of the physics of electricity, definitions of electrical units and terminology, short descriptions of various sources of supply and medical batteries and accessories. The various modifications of the constant current in medical application are touched upon, including the more recent high frequency and sinusoidal currents. The chapter on action of electricity on the body is followed by others on electro-diagnosis, surgery and general therapeutics. The final chapter on special therapeutics is very good and contains many valuable hints. One difficulty that the book offers is that the instruments described differ often from those in common use in this country. One method of application especially in vogue in England—the electric bath in its various modifications, we would do well to use more frequently on this side of the water. The book closes with the usual Erb diagrams of motor points, although Erb is not mentioned, and several diagrams of cutaneous innervation.

The book may be particularly recommended in spite of its too frequent typographical errors, to third and fourth year medical students not intending to specialize in neurology, who wish only a short compendium of electro-therapeutics.

W. B. C.

Surgery: Its Principles and Practice. In five volumes. By 66 eminent surgeons. Edited by W. W. KEEN, M. D., etc. Vol. I, Octavo of 983 pages, with 261 text-illustrations and 17 colored plates. *(Philadelphia and London: W. B. Saunders Company, 1906.)*

This is the second large "practice of surgery" which is appearing at the present time in the United States, and whether it may be the publishers or the profession who demand such works, it is difficult to state; but it seems a pity that these two rival publications should be in the market at the same moment. Bryant and Buck's is to comprise eight volumes, and will, therefore, be somewhat more comprehensive than Keen's, but whether it will be more popular remains to be seen. With men like Mumford, Crile, Bland-Sutton, Adami, the two Da Costas, Frazier, and Martin contributing to the first volume of Keen's "Practice of Surgery," its success should be assured, if the remaining volumes are written by surgeons of equal merit and renown. Although, as has often truly been said, "comparisons are odious," yet it seems fair to express an opinion of preference for Keen's work in certain particulars. The volume is less bulky and more easily handled than that of Bryant and Buck, which is distinctly clumsy. Keen's is equally well printed, and its illustrations appear superior. The reviewer also thinks it an advantage to find a bibliography at the end of each article, as in the work under review, which is missing in Bryant and Buck. It may be considered certain that under Keen's able editorship this practice will hold a high place among systems of surgery, and that it will represent the most advanced knowledge of the day in this branch of medicine. The first volume deserves much praise, and is to be recommended in every respect. R. N.

The Practitioner's Medical Dictionary. By GEORGE M. GOULD, A. M., M. D. *(Philadelphia: P. Blakiston's Son & Co., 1907.)*

Dr. Gould's industry is indefatigable and in addition to numerous other dictionaries, and many volumes of essays, he has found time to prepare another medical dictionary, which in his preface he says "is in every respect and detail new." His competence in this line of work is so well known and so thoroughly appreciated, that it is quite certain that this work will be widely adopted by the profession. The volume is well printed, and light in weight, which is a very great advantage. In regard to some of the illustrations their value seems problematical, but as this is a question on which different opinions may well be held, no stress need be laid on the point in view of the general excellence of the book. It has special advantages over some of the other dictionaries in the addition of "the metric system of weights and measurements of doses"; in the use of the "(B. N. A.) anatomic nomenclature"; and in "the distribution in alphabetic order of eponymic terms." There is no better dictionary of medical terms for the laity. R. N.

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THE ORGANIZATION OF THE LABORATORIES IN THE MEDICAL CLINIC OF THE JOHNS HOPKINS HOSPITAL.

By Lewellys F. Barker, M. D.,

Professor of Medicine, Johns Hopkins University.

Ever since the opening of the Johns Hopkins Hospital the importance of the work of the clinical laboratories has been emphasized. The personal interest and enthusiasm of Dr. Osler in the clinical laboratory work led the members of the medical staff from the beginning to value laboratory investigation as an indispensable accompaniment of the work in the wards. At first the laboratory work consisted in routine examinations and special investigations carried out in small clinical laboratories under the medical wards. For some of the clinical problems attacked these small laboratories were soon found to be insufficient, and in the early years of the clinic, thanks to the courtesy of Dr. Welch, some of the more difficult clinical laboratory investigations were carried on in the pathological laboratory of the university and hospital.

After the medical school was opened the urgent need of facilities for the instruction of medical students in the methods of the clinical laboratory, methods the growing importance of which all recognized, soon became obvious, and special clinical

laboratories were built near the wards for the purpose, the idea being to give every third and fourth year student in the medical school his own laboratory place and outfit for microscopical, chemical, and physical work on materials derived from patients in the wards. In the third year each student is given a systematic training in the use of modern clinical laboratory methods, and in the fourth year the student uses the methods he has learned for the actual investigation of the individual cases assigned to him in his practice as clinical clerk.

This clinical laboratory for instruction, first under the charge of Dr. Thayer, and later under the guidance of Drs. Futcher, McCrae, Emerson, and Boggs successively, has undoubtedly been one of the most important agencies in the education of the students of the Johns Hopkins Medical School; it has been possible as a result of its development to carry on the work at the bedside on a much higher plane than would have been possible without it.

It was soon found that, valuable as such routine clinical laboratory work is for diagnosis and therapy, and contributory as it is to the advance of knowledge by the statistical method, it must be supplemented by original experimental research in order that new methods may be devised and in order that the ever new problems presented by the patients to the clinicians may be solved. From the very beginning of the work of the medical clinic at the hospital the recognition of this investigative, as contrasted with the routine function of the clinical laboratory was appreciated, and the physicians in charge of the laboratory and others associated with them, with the sympathy of Dr. Osler, and largely at his direct suggestion, engaged from time to time in original inquiries which led to results of importance, many of which are recorded in papers in the *Bulletin* and *Reports* of the Hospital.

The physician in charge of the clinical laboratory resided in the hospital and was closely associated with the other members of the resident staff. A clinical bacteriologist also lived in the hospital, directed the bacteriological work of the wards, and engaged in special clinical bacteriological researches. The clinical laboratory thus won for itself a solid place among the clinical disciplines in the Medical School, and made itself a necessary and integral part of the hospital organization.

During the past two years the clinical laboratory has been still further extended, especially on the side of research. In this extension, internal medicine has been influenced by the example of other departments of applied science. Technology has demonstrated how necessary it is for the promotion of the industrial arts to secure investigators trained in the so-called "pure sciences" of physics, chemistry, and biology who will devote themselves to the application of the methods and principles of these sciences to the solution of the special problems by which those who wish to advance the industrial arts are confronted. One has only to recall the tremendous advances in metallurgy, in brewing, in electrical engineering, in the manufacture of arms and ammunition, in sugar refining, and in food preservation to realize how fundamentally significant the interesting of men trained in pure science in the solution of the so-called "practical problems" has been for the extension of knowledge and practice in more strictly utilitarian domains.

Since von Ziemssen recognized the need for similar applications of the fundamental sciences to the solution of the special problems of diagnosis and therapy, and founded clinical research laboratories at the hospital in Munich, the idea has spread, until to-day the work of research by internists in laboratories adjacent to their wards is regarded as essential at least in university clinics.[1] It has occurred to me that a brief description of the organization of the general and special laboratories in the department of medicine at the Johns Hopkins Hospital might be interesting to those who have developed similar laboratories elsewhere and especially to workers in internal medicine contemplating such a development.

The laboratories consist of a general clinical laboratory for instruction and research, laboratories for the routine work of the wards, special laboratories for the application of biological, physiological, and chemical methods to the solution of clinical problems and certain other laboratory facilities to be mentioned further on.

The General Clinical Laboratory for the Instruction and Research and the Routine Ward Laboratories.

(Dr. Thomas R. Boggs in Charge.)

This laboratory, the nucleus of all the clinical laboratories and about which the others cluster, is situated on the second and third floors of the dispensary building and is in direct connection with the biological and clinical divisions and with the wards and outpatient department.

The equipment comprises two large general laboratories for the accommodation of the students where each member of the third and fourth year classes has a locker and desk space. There are in addition, a stock room for supplies or reagents and apparatus of all kinds used in the varied instructive, routine and special work. A general preparation room with Kjeldahl installation and a dark room for spectroscopic and polariscopic work and three rooms for special workers are included.

The functions of the laboratory are two-fold: (a) to give the students a thorough training in the application of all laboratory methods to the diagnosis and investigation of disease. The course extends over the entire academic year and the immediate connection of the laboratory with the wards and the out-patient department makes available an unusually large and varied material. Incidentally this use of the ward material is of no small value to the clinic in diagnosis. For with the simultaneous examination of material by a large number of observers a diagnosis is not infrequently reached which had been overlooked in the more limited examination possible in the wards. (b) The second function of the laboratory is the encouragement of investigation. We are able to offer to special workers laboratory facilities and clinical ma-

[1] Cf. Welch (W. H.). The Evolution of Modern Scientific Laboratories. Johns Hopkins Hos. Bull., Balto., 1896, vii, 19-24.

terial for study along varied lines of medical interest, especially for the study of groups of cases with regard to questions of diagnosis and the results of therapeutic measures.

The development, criticism, and practical application of new methods may here be undertaken to advantage. In addition to this we are able to afford students on the wards special opportunity for detailed study of cases under their charge.

The Routine Laboratory of the wards is also under the direct charge of this department. It has just been entirely remodeled and comprises three laboratory rooms and a stock room. These laboratory rooms are all finished in white tile wainscot and polished cement floors; and have slate-topped tables. Room A is the laboratory for qualitative urinary studies where the routine examination of the specimens from the wards supervised by the resident physician, Dr. Emerson, is conducted by the house officers and the fourth year students. It is equipped with microscopes, centrifuge, and reagents necessary for all ordinary tests.

Room B is devoted to the quantitative work of the routine of gastric analysis, of the determination of sugar, chlorides, and other quantitative analyses ordinarily applied to the ward cases. Special lockers are provided equipped for the different procedures indicated, and the student has the sole use of one of these while he is studying a given case.

Room C is for the study of sputum only, and here all examinations from the hospital and out-patient department are made. No other work is permitted here. Only necessary tables, sinks, and staining appliances are permitted in the room, which is also equipped with a large high-pressure autoclave for the sterilization of the vessels, plates, etc. Adequate provision for the cleansing and disinfection of the hands is also made.

This laboratory for routine work is a natural and valuable feeder to the department of instruction and research in the General Laboratory and the students are encouraged to carry out any investigations requiring more special appliances in the latter.

The Biological Laboratory of the Medical Clinic.

(Dr. Rufus I. Cole in Charge.)

Three rooms on the second floor of the surgical building are at present used as a laboratory. A large corner room with windows on two sides offers accommodation for about eight workers. A smaller room adjoining is used by Dr. Cole and one research worker, while a third room is used by the assistant in charge of the routine bacteriological work of the medical department of the hospital. A vault which adjoins these rooms, and which was intended as a receptacle for the medical histories, but which is not needed at present for this purpose, is used as a centrifuge room, as it is found that the noise and vibration is disturbing when the centrifuge is in the same room with workers. The equipment includes an ordinary small electric centrifuge, and also a larger one which revolves eight 25 cc. tubes, with a speed of 3000 revolutions per minute. Such a large centrifuge is necessary in precipitating bacteria from suspensions. In the main room of the laboratory are two large thermostats for the use of workers, and this room is also equipped with lockers and media-closets. Sterilizers and all the apparatus necessary for ordinary bacteriological and biological investigation are kept on hand, and special apparatus required by workers for carrying out their investigations are supplied.

A small animal house for holding a limited number of smaller animals, with yards in which they can be given exercise in the open air, has been built on the hospital grounds. A house for larger animals is needed and will doubtless be supplied as the work progresses. In all experimental work the importance of having the animals kept under good hygienic conditions cannot be over-emphasized.

The purpose of the laboratory is to investigate biological methods of diagnosis and treatment. The possibilities of refinements of diagnosis which the more recent studies of immunity have afforded, make it necessary that these methods should be investigated with the object of rendering them of practical application in the clinic. Such studies also, even if not of immediate practical application, are of great value in adding to our knowledge of the pathogenesis of acute infections. Knowledge of this kind is necessary before we can have any rational specific treatment in the great group of infectious diseases; the discovery of new facts along these lines brings the attainment of this end nearer. There is, therefore, the best of reasons for the establishment of biological laboratories in direct connection with medical clinics. While the problems investigated may at times seem far removed from immediate application to diagnostic and therapeutic purposes, yet it is only by careful investigation of the problems, in immediate contact with a medical clinic, that the applicability of new discoveries can be brought home to the minds of clinical men. In this work there is always a marked tendency to make immediate practical application of results; it should be the purpose of the clinical laboratories to see, first, that methods so applied are based upon sound scientific principles, and secondly, by controlling their actual use upon patients, to determine their real value. The importance, therefore, of men who have been trained not only in special science but also in clinical observation undertaking the solution of such problems is obvious. At present the investigation of methods of specific treatment is left too largely in the hands of manufacturers, whereas it should be the function of the research laboratories of departments of internal medicine. Considerable expense is involved in investigations of the kind mentioned, and it will of necessity be some time before there will be many well-endowed laboratories which can undertake extensive experiments along these lines.

During the past year, on account of the great interest which was stimulated in the opsonic theory and method of treatment by vaccines by the lectures and work of Wright, a considerable part of the work of the biological laboratory in this clinic has dealt with an investigation of problems bearing on this theory.

The biological division of the laboratory is open to all those who are fitted to do experimental biological work, and who are

interested especially in problems pertaining to internal medicine. This year a practical course in immunity was offered to ten students. These men performed the more fundamental immunity experiments; later certain of them undertook the solution of special problems, work upon which is still in progress.

The laboratory offers facilities to members of the medical staff who desire to undertake especial researches, either in connection with patients or upon animals. For such work (especially for those spending much time at the bedside) a thoroughly organized laboratory with easy facilities is indispensable. The laboratory attempts to make its methods and materials easily accessible to qualified inquirers. Post-graduate students working in medicine who desire to spend all or a part of their time in clinical biological reasearch will have problems suggested to them and will be aided in solving them. While the futility of physicians with little preparation (or of those who can devote but a short time to work) undertaking work on such problems is fully realized, those who have adequate preparation, the necessary leisure and a real desire to assist in the discovery of new knowledge are given opportunities and are encouraged.

The special advantages which the laboratory offers to students and physicians working upon the problems of infection and immunity are: (1) Its close association with the medical wards of the hospital, so that clinical material is always available, and (2) the intimate association of its work with that of the medical staff as a whole so that the clinical bearing of new scientific truths is quickly recognized. The division of the laboratory, though only recently established, has already made itself an important part of the medical clinic.

The Physiological Laboratory of the Medical Clinic.

(Dr. Arthur D. Hirschfelder in Charge.)

The physiological division of the clinical laboratory was organized in October, 1905, for the purpose of studying both individual cases and diseased conditions from the standpoint of disturbance of function. It is provided with two small laboratories: One in the New Surgical Building of the Hospital for the clinical study of patients by the special methods in use in physiological laboratories, particularly the graphic methods; the other work-room is in the Hunterian Laboratory of the Medical School. The latter is well equipped for animal experiment, and there the diseased conditions seen in the wards may be reproduced in animals and studied by physiological methods. As far as is possible this is done with a view to establishing by animal experiment the procedures of a true physiological therapy. It has been the aim in this laboratory to bring the studies upon the patient as closely as possible into relation with the findings upon animals and upon mechanical models and to turn these results to practical use. Our experience has fully demonstrated that the best results of animal experimentation are obtained when they are subjected at once to the test of comparison with the conditions found in the patient.

Investigations have been carried on thus far upon some of the problems of secretion by the kidney in experimental nephritis, upon the graphic study of the venous pulse, upon numerous disturbances of cardiac function, paroxysmal tachycardia, Adams-Stokes Disease, and particularly upon the conditions in aortic insufficiency which determine the form of the pulse wave, the variations in maximal and minimal blood-pressure and the failure of the heart. It is hoped in the future to extend the scope of the investigations to the disturbances of secretion and to the study of the pathological physiology of the nervous system, making use of the methods of modern experimental surgery in reproducing, studying, and remedying the conditions.

Optional courses upon the physiological aspects of the diseases of the circulatory system have been offered for students and post-graduates; the disturbances of function are shown as far as possible (1) upon the patient and (2) upon the animal with the structures exposed. Whenever possible the two demonstrations are made upon the same day, otherwise they are made upon successive days; for it is thought that a far better understanding of the clinical condition can be obtained when the experimental picture is fresh in the mind. Further, many minor and even major problems arise at the bedside, which can by laboratory investigation receive elucidation not otherwise possible. It is hoped that in the future the students may be more and more encouraged to look upon their ward and dispensary patients from the physiological standpoint and to investigate the problems arising in their personal experience by the experimental methods.

The Biochemical Laboratory of the Medical Clinic.

(Dr. C. Voegtlin in Charge.)

It is well recognized at the present time that chemistry plays an important rôle in modern medicine. It should be, therefore, the aim of every large hospital and medical school to promote by its aid the more accurate diagnosis and the better treatment of disease. These purposes, however, are by no means easily accomplished because of the relatively elaborate needs that such an undertaking requires. Chemical work is largely dependent upon a laboratory that is furnished with the varied apparatus and materials used in this science. Further, to be of full value to the medical clinic of a hospital, a chemical laboratory must be situated within the walls of the institution, with easy access to the wards, the chemist in charge must have been thoroughly trained in the pure science and he and the members of the hospital staff should be always in close touch. With these ideals in view, and with the support of the hospital and university and of a generous donor who desires that his name shall not be mentioned the biochemical division of the laboratory of the medical clinic of the Johns Hopkins Hospital has been equipped with accommodation for eight workers. Since the establishment of this laboratory last year the work has consisted in investigations bearing upon problems of metabolism, and especially upon the regulation of diet in various diseases, *e. g.*, typhoid fever, nervous diseases, diabetes, and gout. The influence of certain drugs upon the organism, a subject which offers still a large

field for scientific experimental work, is being taken up. The metabolism is studied in cases in which a clinical diagnosis is uncertain or where there are signs of disturbed assimilation of the food or pathological changes in the excretion of the metabolic end-products of the body. Besides this, parts of various organs, that may have been removed from the body as well as blood, exudates and other fluid can be analyzed with the aim of assisting the diagnosis and therapy of special cases.

The value of this kind of work is two-fold. First, it is of benefit to the patients; second, physicians and advanced students are afforded the opportunity of becoming familiar with the general principles of metabolism and nutrition, a subject that is of the utmost importance and one which has hitherto been too much neglected by the medical profession at large.

The chemical division of the clinical laboratory is well equipped for its especial work. The general outfit, though in miniature, is modelled upon the arrangements in the first chemical institute in Berlin, as many conveniences and time-saving devices as possible having been introduced. The facilities for hydrolysis, vacuum distillation, ether recovery, evaporation, combustion, calorimetric work, nitrogen determinations, etc., are very satisfactory. The laboratory is supplied with a liberal variety of Kahlbaum and other pure chemicals, and efforts are always made to provide the special apparatus and supplies which a particular investigation may require.

The work of the past year has led to publications of importance and it is hoped and believed that the inauguration of this division of the clinical laboratory marks an important step forward in the ever-increasing division of labor and specialization which the expansion of the modern medical clinic necessitates.

Other Laboratory Facilities in the Medical Clinic.

Though the description of the laboratory facilities of the medical clinic here given deals with the clinical laboratories proper, it would be wrong to allow the opportunity to pass without reference to the continuous advantages to the clinic since the opening of the hospital of the close cooperation between the pathological laboratory of the university and hospital and the wards. The pathological laboratory has been and is still the fountain-head of inspiration for our whole medical organization. Aside from the all-important control of the clinical work by thorough post-mortem examinations the laboratory by its histological, bacteriological, and parasitological studies in connection with the wards, performed, in the earlier days of the hospital, the functions of a true clinical laboratory, and by its more recent expansion at the Hunterian Laboratory in the field of experimental pathological physiology, and experimental surgery it promises to be of even greater service than ever to the allied clinic. A notable innovation, and one which has already proven of great advantage both to staff and students, has been the conduct by Professors Thayer and MacCallum of a clinical pathological conference on Monday afternoons, during which the histories, and intra vitam diagnosis of the clinic are compared (and, when necessary, contrasted) with the findings of the autopsy table.

The laboratories of anatomy, physiology, and pharmacology have also each contributed directly to the work of the medical clinic. A course in clinical medical anatomy is given in the anatomical laboratory, members of the physiological staff have conducted investigations in the wards on blood pressure, on heart block, and on Cheyne-Stokes breathing, and the physiological chemists and pharmacologists have on request helped the workers in the medical clinic in spectroscopic and other special examinations. Without the hearty cooperation and willing self-sacrifice of the various workers in these laboratories devoted to the fundamental medical sciences much that is being accomplished in the work of the medical wards and laboratories would be impossible.

The X-ray laboratory, in charge of Dr. F. H. Baetjer, though primarily a part of the surgical organization of the hospital, has been of very great service to the medical clinic also. In the various forms of arthritis, in diseases of the bones and spine, in gastric and œsophageal disease radiography has been most helpful in diagnosis. Fluoroscopic examinations are now a part of the regular routine in all obscure intrathoracic conditions and the diagnosis of aortic aneurism is now made so easy that there is some danger of neglect of the older methods of arriving at a positive diagnosis of the condition.

For the therapy of the medical clinic the X-ray laboratory has also been drawn into service (skin lesions, exophthalmic goitre, unresolved pneumonia).

The electrodiagnostic and electrotherapeutic laboratory of the clinic form a part of the equipment in the department of neurology of which Dr. H. M. Thomas has charge.

Two additional laboratories are much needed in the medical clinic, one for the study of tuberculosis in the Phipps Dispensary in charge of Dr. Louis V. Hamman, and the other a psychopathological laboratory for the investigation of the psychic side of the cases in the medical wards.

Rooms for the laboratory for the study of tuberculosis are already provided in the Phipps Dispensary and a further sum of money for laboratory purposes has just been donated by the generous giver to whom the medical clinic of the hospital owes this important foundation. This sum, together with the gifts of other friends of the movement to study tuberculosis here, will make it possible to develop the much-needed laboratory side of our tuberculosis work.

At present no funds are available for a psychopathological laboratory. Rooms for the purpose and a laboratory leader trained in the modern methods of the psychological laboratory and especially one versed in the art of psycho-analysis are urgently required, especially pending the endowment and development of that institution so urgently needed here in Baltimore, a university psychiatric clinic.

Enough has been said to make clear the rapid expansion of the clinical laboratory and the benefits to be derived by the clinic from its further growth and work. The papers pub-

lished in this number of the BULLETIN, though representing only a part of the original investigation carried on during the past year, are sufficient to illustrate the character, aims, methods, and results of the laboratory inquiries. The work is still hampered by lack of funds. The time has come when a building of considerable size is needed to house the clinical laboratory and its various subdivisions in order that they may meet the pressing demands that are being made upon them. An endowment which would permit the erection of such a building, equip it, supply salaries for leaders trained in the special sciences so that they can devote their whole time to the work, and meet the annual supply and expense budget would require the setting aside of a large amount of money. Here, surely, is a tempting opportunity for some liberal-minded man or woman who desires to benefit mankind by increasing diagnostic precision and enhancing therapeutic skill.

NOTE ON THE OCCURRENCE OF HOWELL'S NUCLEAR PARTICLES IN EXPERIMENTAL ANÆMIA OF THE RABBIT AND IN HUMAN BLOOD.[1]

By ROGER S. MORRIS, M. D.,

Assistant in Medicine, The Johns Hopkins University; Assistant Resident Physician, The Johns Hopkins Hospital.

(*From the Laboratory of the Medical Clinic.*)

In 1890 Howell (1) discovered in the blood of cats, following a severe hæmorrhage, that a majority of the red blood corpuscles may contain "a single good-sized piece of nuclear matter, too large to be called a granule, but having the shape and appearance of a large nucleolus." This fragment stained readily with methyl green, like the nucleus; it could be seen also in the unstained corpuscles as a refractive particle. It was noted that "the fragment of nuclear matter always lay imbedded in the periphery of the spherical corpuscle." The fragments could not be detached from the corpuscles by shaking or by the addition of water, acetic acid, or other reagents which dissolve out the hæmoglobin of the cell. Moreover, the fragments were not found in the blood of cats normally, but usually followed a severe hæmorrhage. "The only satisfactory explanation of the phenomenon which has occurred to me is that the fragment is a bit of the nucleus left adhering to the corpuscle at the time that the nucleus escaped. Under the conditions necessary for the appearance of the phenomenon, we may suppose that the process of production of new blood cells was vastly accelerated, and that therefore the extrusion of the nucleus was not as perfect as under normal conditions." (Howell.)

Schmauch (2) was the second to study these bodies in the blood of the cat. He called them "endoglobuläre Körperchen." They were found in large numbers (80 per cent of the corpuscles) after venesection and in poisoning with pyrodin and with extract of bothriocephalus latus. In the fresh blood the nuclear particle was seen to vary much in size, from a scarcely visible granule, through all stages up to the size of a nucleus, and to be either round or irregular in shape; some of them showed motility in the fresh blood, usually those which were irregular in form. Fixation of the specimen caused the "endoglobular particles" to shrink, and they were usually round or oval, or possessed of one or two projecting processes. No specific stain could be found for these bodies, but they were stained with all nuclear dyes. The red blood cells which contained the "endoglobuläre Körperchen" presented no abnormalities in form, size, or hæmoglobin content. Erythrocytes possessing nuclear particles were found in all of the internal organs, when present in the peripheral circulation; no local increase in their number was found in any organ or tissue. In a few animals, bone marrow was removed under anæsthesia; no difference was discoverable between it and the circulating blood in the number of red blood cells having nuclear particles. Schmauch believed, in view of the transitions in size from the fully developed nucleus to the smallest "endoglobuläre Körperchen" and the similarity in staining reactions, that these bodies were nuclear in origin and that the loss of the nucleus in the red blood cell of the cat is accomplished not by a breaking up of the nucleus into granules, but rather by a gradual shrinking.

Pol (3), in a study of the pathological morphology of the erythrocytes of the rabbit after phenylhydrazin poisoning, described in a few of the red blood cells "a single, somewhat excentrically placed, coarse, round body, staining intensely with nuclear dyes," which he identified with that found by Schmauch in cats, and by Schmidt (4) in rabbits during poisoning with phenylhydrazin. Schmidt saw similar bodies in the blood of new-born rats and of adult mice. Jolly (5) has also called attention to their constant presence in the blood of new-born white rats and mice; they disappear from the circulating blood shortly after birth. He has found them in the embryo of the white rat and of the mouse (6), and believes, as does Schmauch, that they originate from atrophy of the nucleus.

In the blood of rabbits poisoned with pyrodin (see article in this number of the BULLETIN) I have also met with these small nuclear particles, first described by Howell, in the red

[1] Presented at the Meeting of the American Association of Pathologists and Bacteriologists, at Washington, May 7, 1907.

1. Normal red blood cell.
2. Rabbit. Polychromatophilic red cell containing nuclear particle.
3-13. Pernicious anæmia: 3-5 red blood cells containing single nuclear particles; 6-9, red blood cells containing multiple nuclear particles; 10, 11, red blood cells containing a nuclear particle and basophilic granules; 12, nucleated red blood cell containing two nuclear particles and basophilic granules; 13, megaloblast containing two nuclear particles.
14, 15. Human embryo. Red blood cells containing nuclear particle.
16-18. Typhoid fever (blood crisis): 16, crenated red blood cell containing nuclear particle; 17, polychromatophilic red blood cell containing a nuclear particle; 18, normoblast containing a nuclear particle.
All stained with Hastings' modification of Romanowski's stain.

blood cells. They are, as a rule, very few in number, though occasionally there is a crisis, as many as six having been found in one field (Leitz oil immersion). They do not occur in the blood of normal adult rabbits, so far as I have been able to observe, but may be seen after anæmia becomes established, usually after the count has fallen to about 3,000,000 red blood cells. Their appearance is coincident with that of basophilic granules in the red blood cells, though the cells possessing basophilic granules greatly outnumber those with nuclear particles. The latter were not observed in the fresh blood because of their paucity, but in stained preparations (Fig. 2) they were almost invariably excentrically placed, round or oval in shape—rarely irregular, single (though as many as three have been found in one cell, their size varying considerably); their outline was very sharply defined and occasionally there was noted a paler zone in the protoplasm of the red blood cell surrounding the nuclear particle. They were found in normally staining red blood cells and in those showing polychromatophilia. One fact which was striking in many preparations was the almost complete absence of the deformity (degenerative change) characteristically produced by phenylhydrazin and its derivatives in those cells which contained either a nuclear particle or basophilic granules; this rule was not without exceptions, but it held good in the great majority of instances. The nuclear particles were found rarely in cells possessing a nucleus and in those possessing basophilic granules. Unlike the basophilic granules, the nuclear particle takes on a purple color like that of the nucleus with Romanowski stains. With Ehrlich's triple stain, it seemed that fewer nuclear particles were visible than with hæmatoxylin or with methylene blue.

In the blood of man, Howell's nuclear particles have not been described, so far as I know. In the blood of a patient (A. H., Gen. No. 58,647), recently admitted to Dr. Barker's service, suffering with pernicious anæmia, large numbers of these bodies have been found (Figs. 3 to 13). They were present during and after a blood crisis, in which large numbers of intermediates and megaloblasts, as well as normoblasts were found in the circulating blood (to be reported later by Dr. Krause). The preparations studied were stained with Hastings' stain (modified Romanowski). The nuclear particles resembled morphologically those seen in the rabbit in every particular; but cells containing two or more nuclear particles were very much more numerous here than in the blood of the rabbit (Figs. 6-9, 12, 13). Again, with Hastings' stain, a few nuclear particles were found beautifully stained a brilliant violet (Figs. 5, 7, 10, 11). The majority of the cells containing nuclear particles were of normal or increased size, though many microcytes were seen to possess them, and in most instances the cells with nuclear particles were polychromatophilic, often markedly so, as shown in the accompanying plate. Not infrequently a nuclear particle, often stained violet, was found in a red blood cell with many bluish granules (Fig. 10, 11, 12); the presence of both in the same cell was rare in rabbit's blood. Nucleated red blood cells frequently contained one or more nuclear particles; in some instances the nuclei were fragmenting (Fig. 12), and a filament connecting one or more of the nuclear particles with the larger mass of the nucleus was visible; but usually the particles appeared entirely separated from the nucleus. It is not only in cells having fragmenting nuclei, however, that nuclear particles may be encountered; they have been found in cells with active, perfectly intact nuclei. One megaloblast was found showing a fine chromatin net-work in the nucleus, with two nuclear particles in the surrounding protoplasm (Fig. 13). The presence of such particles in a cell with intact nucleus is of some importance, in that one of the chief arguments against the nuclear origin of the basophilic granules is their occurrence in cells possessing active nuclei. It by no means proves the nuclear origin of the basophilic granules, but it does lessen the value of the argument mentioned. The occurrence of a nuclear particle and basophilic granules in the same cell, does not necessarily mean that the latter are degenerative changes. Nuclear particles are often found in nucleated red blood cells, and it is conceivable that the larger part of the nucleus in such a cell may break up into fine basophilic granules. In man, the nuclear particles are so frequently found in cells having nuclei that their origin through atrophy of the nucleus, as Schmauch and Jolly consider likely in animals (cat, rat, mouse), can be excluded in at least a part of the instances. That both methods of formation may hold good in man is quite possible, *i. e.*, (1) atrophy of the nucleus, or (2) a body derived from the nucleus.

Having seen nuclear particles in the blood of pernicious anæmia associated with a blood crisis, it seemed likely that they would be found in other conditions in man, in which a large number of nucleated red blood cells appeared in the circulating blood. It was not surprising, therefore, to find them in the blood of the human embryo. They were present in small numbers in two cases examined (Figs. 14, 15); one a fœtus 15 cm. long (mother had acute lymphatic leukæmia), the other a fœtus 15 cm. long (mother a healthy colored woman). Furthermore, similar nuclear particles were found in the circulating blood in a patient (Wm. C., Gen. No. 56,567), suffering with typhoid fever, in whose blood there occurred a remarkable crisis with a large number of nucleated red cells (case to be reported in detail by Dr. Emerson). Finally, Dr. Boggs has recently shown me Howell's nuclear particles in the blood of an infant, aged 7 months, suffering with anæmia pseudo-leukæmia infantum; in the blood there were present about 25,000 nucleated red blood cells per cubic millimeter.

The occurrence of nuclear particles in human blood has been associated with the presence of a large number of nucleated red blood cells, *i. e.*, coincident with increased blood formation, as in animals. These bodies are to be looked upon as a sign of regeneration of the blood, cells containing them probably being younger forms of the red blood cell. The nuclear particles in the nucleated red blood cells resemble closely the "basophilic granules" which occur in some of the

lymphocytes in the circulating blood and suggest the possibility of the nuclear origin of the latter.

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BLOOD FORMATION IN THE LIVER AND SPLEEN IN EXPERIMENTAL ANÆMIA.[1]

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It is a well-established fact that the chief function of the bone marrow in adult life is hæmatopoiesis. In embryonic life the liver and spleen are hæmatopoietic organs, but in extrauterine life the marrow unaided seems to be adequate for the formation of the blood and this function is then lost by the liver and spleen, which differ in a corresponding way histologically at these two stages of life. Shortly after birth there is apparently less need for rapid production of blood corpuscles than in the embryo, and this results, therefore, in the absence of recognizable hæmatopoietic (myeloid) tissues in liver and spleen, while at the same time evidence of extensive proliferation is less marked in the bone marrow. If, however, unusual demands are made upon the bone marrow for one reason or another, as, for example, through the loss of a large quantity of blood from hæmorrhage, signs of increased activity are found; and in certain instances, as in most cases of pernicious anæmia, the alteration of the marrow may be such that it resembles in a remarkable manner that seen in the embryo—a reversion of the marrow to the embryonic type, as Ehrlich pointed out many years ago. Here, to all intents and purposes, the problem of the pathological physiology of blood formation in severe anæmias has remained until the recent publications by Meyer and Heineke (1, 2) of the results of their studies, which prove, they believe, a similar reversion to the embryonic type on the part of the liver and spleen in cases of grave anæmia.

In a careful examination, both clinical and histological, of 11 cases of severe anæmia (1) which came to autopsy (seven cases of pernicious anæmia, two of anæmia following sepsis, one of anæmia associated with cardiac disease, and one of so-called leukanæmia) and, in their second more complete study (2), of an additional two cases of pernicious anæmia diagnosed at autopsy, Meyer and Heineke have found strong evidence of blood formation in the liver and spleen. The organs were studied from smears made from the freshly cut surfaces post-mortem and from histological sections. In the spleen they found alterations in all instances; these consisted in decrease in size of the follicles and collections of mononuclear cells, varying greatly in size and in the relation of nucleus to cell body, within the venous sinuses—the so-called Billroth's veins of the spleen. These cells they identified from a study of the smears and sections, as normoblasts, myelocytes, and mononuclear, non-granular, "lymphocyte-like" cells. Changes in the liver were not so constantly present, but were found in seven cases. They were of two kinds: (a) In three instances they found groups of mononuclear cells collected in the liver capillaries, chiefly in the peripheral portion of the lobules, consisting of lymphocyte-like cells, normoblasts, and myelocytes, and (b) in four cases there were collections of large mononuclear cells rich in protoplasm in the periportal connective tissue, usually arranged about the vessels, with many mononuclear eosinophile cells also. In the smears made from both spleen and liver the proportion of nucleated red blood cells and myelocytes greatly exceeded that found in preparations made from the blood. The liver sections corresponded very closely in appearance with those of the human embryo's liver at about the seventh month, while the spleen was also embryonic in type. No collections of cells like those described in the liver and spleen were found in any other organs, and the authors felt justified in the belief that the changes represented true blood formation rather than a wandering in of cells from the circulation, the cell-nests resembling closely those seen in the bone marrow.

With the view of determining whether similar changes could be reproduced in animals by the administration of substances known to cause anæmia, experiments were begun by the writer at the suggestion of Prof. Müller and Dr. Meyer. The rabbit was the animal chosen and pyrodin (acetylphenyl-

[1] Presented before the American Association of Pathologists and Bacteriologists at Washington, D. C., May 7, 1907.

[2] These experiments, begun in Prof. Müller's laboratory, have been continued in the laboratory of the medical clinic of Prof. Dock of the University of Michigan and in that of Prof. Barker of Johns Hopkins University.

hydrazin) was selected as the toxic agent. The attempt was made to produce a chronic anæmia of rather severe grade, so that the bone marrow would be overtaxed in blood formation. By this means it was hoped that the liver and spleen would reassume one of their embryonic functions and assist in the production of blood.

The animals were kept in well-cleaned and ventilated cages and were fed with oats and greens daily. Frequent examinations of the blood were made, including counts of both red and white cells, estimation of hæmoglobin, and smears. Pyrodin was given about 5 p. m., the dose depending upon the blood count made earlier in the afternoon. A solution of pyrodin in water was prepared in which 1 cc. equaled 0.005 gram pyrodin.

Experiment A. Rabbit I. Male. Weight, 2665 grams. Pyrodin administered by stomach tube.

Date. 1905	R. B. C.	W. B. C.	Hb.		Pyrodin	Remarks
30-VI	5,550,000	12,000				
3-VII	5,200,000	7,080			0.015	
4-VII					0.01	
5-VII	5,350,000	9,600	60%	(Sahli)	0.02	
6-VII	4,090,000				0.02	
7-VII	3,650,000	14,732	43%	"	0.03	
8-VII	2,875,000				0.02	
10-VII	2,105,000	17,166	25%	"	0.02	No free Hb. in serum.
11-VII	2,200,000				0.02	
12-VII	2,155,000	11,776	17%	"	0.02	
13-VII	1,830,000				none	Animal weak. Wt. = 1964 gms.
14-VII	1,940,000	13,954	25%	"	"	
15-VII	2,375,000	11,354	31%	"	"	
17-VII	2,435,000	5,820	46%	"	0.02	
18-VII	3,490,000	5,154	46%	"	0.03	Fresh solution of pyrodin.
19-VII	3,125,000				0.035	Serum clear.
20-VII	2,635,000	8,660	37%	"	0.03	
21-VII	2,265,000				0.03	Serum faintly pink.
22-VII	1,910,000	15,466	26%	"	0.03	Abscess of left ear.
24-VII	1,080,000	18,688	25%	"	none	
25-VII	1,930,000				0.03	
26-VII	1,937,000	9,622	34%	"	0.03	
27-VII	2,245,000				0.04	
28-VII	1,785,000	12,622	31%	"	0.03	Fresh solution of pyrodin.
29-VII					0.02	
30-VII	1,875,000	11,266	29%	"	0.03	
31-VII	1,230,000				0.02	
1-VIII	1,450,000	33,822	23%	"	0.025	Ear abscess evacuated.
2-VIII	1,925,000				0.03	
3-VIII	1,565,000	8,600	23%	"	0.03	
4-VIII	1,385,000					Died.

Death occurred some time between 11.45 a. m. and 2.45 p. m. At autopsy the body was warm. There was slight rigor mortis in the legs. Weight = 2065 grams. All of the organs were very dark in color. The spleen was enlarged, measuring 8 x 1.5 x 2 cm. The bone marrow was dark reddish brown in both femurs. The lungs were air-containing throughout and there were numerous pin-head hæmorrhages on the surfaces. The kidneys showed pigmentation of the cortex; this was especially marked along the inner edge. Heart muscle was paler than normal. There was very little blood in the organs. No fluid in peritoneum, pleuræ, or pericardium.

MICROSCOPICAL EXAMINATION.—The tissues, fixed in alcohol, mercuric chloride and acetic acid, and formaldehyde, were embedded in paraffin and in celloidin, sectioned, and stained with hæmatoxylin and eosin, van Gieson's stain, and borax carmine with potassium ferrocyanide and hydrochloric acid.

Bone marrow.—The marrow of the shaft of the femur, normally fatty in full-grown rabbits, showed marked hyperplasia, the fatty marrow being entirely replaced by myeloid tissue. A study of smears, stained with hæmatoxylin and eosin, May-Grünwald's stain, and Ehrlich's triple stain, in conjunction with that of the sections, shows that the non-granular mononuclear cells (myeloblasts) are greatly in the majority. There are many normoblasts and many intermediates, but no typical megaloblasts. Myelocytes are also numerous. There are a few phagocytes and many megalokaryocytes (see Fig. 1).

Spleen.—There is marked destruction of the cells of the pulp. The follicles are diminished in size and in some instances the central artery is almost completely devoid of lymphoid tissue. *In the venous sinuses* there are large *nests of mononuclear cells* with non-granular protoplasm and rather deeply staining nuclei (see Fig. 2). There is an enormous number of phagocytes containing fragments of red blood cells and brown amorphous pigment, both in the capillaries and venous sinuses and in the pulp. Megalokaryocytes are fairly numerous. *Smears* made from the freshly cut surface of the spleen show many non-granular mononuclear cells like those in the bone marrow, varying in size from that of a red blood cell to a cell whose diameter is twice as large or greater, the protoplasm being very basophilic, the nucleus a little paler (May-Grünwald stain). Many of the nuclei have brick red blotches which extend at times into the protoplasm. From the former cell one sees apparently all gradations to the typical myelocyte, *i. e.*, from cells having few pseudo-eosinophile or eosinophile granules to those having many. There is a moderately large number of myelocytes. In the smears there are also a few normoblasts. Very few polymorphonuclear pseudoeosinophiles are seen and rarely one finds a mastcell. There are many pale, free nuclei. Phagocytes are present.

Liver.—The section of the liver presents a remarkable picture. The liver cells are well preserved, but show considerable pigmentation, hæmosiderin being present in large amount. The *liver capillaries* are much *widened, and in them, especially in the periphery of the lobules* (see Fig. 3), are *nests of mononuclear cells* (Fig. 4), having non-granular protoplasm and deeply staining nuclei (hæmatoxylin and eosin). The cells of the intracapillary nests resemble large lymphocytes, though at times apparent erythroblasts (normoblasts) and

undoubted pseudoeosinophile myelocytes are seen. Some of the cells show mitotic figures. The number of cells seen in the central veins of the lobules and in the larger vessels of the liver is relatively much less than that in the capillaries of the peripheral part of the lobules, while in the central zone of the lobules nucleated cells are very scarce in the capillaries. Occasionally a *megalokaryocyte* is found, often in connection with a collection of mononuclear cells (see Fig. 5), at times independent of a cell-nest. In the capillaries there are also phagocytes like those seen in the spleen. No collections of mononuclear cells are found in Glisson's capsule, though there is a myelocyte occasionally. *Smears* made from the liver resemble in every way those made from the spleen.

Kidneys.—These organs show no noteworthy alteration except for marked hæmosiderosis of the cortex.

Lungs.—There is moderate congestion. A few megalokaryocytic emboli are seen.

The remaining organs showed nothing of importance.

In this experiment we have, then, a chronic anæmia produced by administration of pyrodin in which a maximal effort has been made on the part of the organism to regenerate the blood. Not only is the bone marrow hyperplastic, but the liver and spleen which present a very striking resemblance to those organs in the rabbit's embryo during the stage when they are actively engaged in blood formation, may be assumed to aid in the formation of blood. The picture parallels that described by Meyer and Heineke in pernicious anæmia in man to a striking degree in the presence of myeloid tissue in both liver and spleen, and further resemblances to pernicious anæmia are found in the high color index which existed during life, the blood crises, the presence of "nuclear particles" in the red blood cells (to be described in another paper), the myeloblastic type of bone marrow, the phagocytosis in the hæmatopoietic organs, and the hæmosiderosis of liver, spleen, and kidneys.

Experiment B. Rabbit II. Male. Weight, 1285 grams. Pyrodin given subcutaneously and by stomach tube.

Date. 1905	R. B. C.	W. B. C.	Hb.	Pyrodin	Remarks.
1–VII	5,200,000	9,000			
3–VII			Gm.	0.01	
4–VII	3,055,000	7,140	40% (Sahli)	0.005	
5–VII				0.005	
6–VII	2,700,000	9,732	32% "	0.005	
7–VII	2,900,000			0.01	
8–VII	2,675,000	14,600	35% "	0.01	
10–VII	2,350,000			0.01	
11–VII	2,655,000	16,110	41% "	0.01	Hb. estimation verified.
12–VII	2,265,000			0.01	
13–VII	2,465,000	8,510	35% "	0.015	Wt. = 1335 gms.
14–VII	2,180,000	10,688		0.01	
15–VII	2,330,000	5,576	37% "	0.015	
17–VII	2,410,000	11,600	36% "	0.02	
18–VII	2,610,000			0.025	Fresh solution of pyrodin.
19–VII	2,585,000	10,844	38% "	0.03	
20–VII	2,160,000			0.02	
21–VII	2,060,000	25,532	32% "	0.025	
22–VII	1,725,000		"	0.02	
23–VII	1,212,000	33,488	26% (Sahli)	none	
24–VII	1,835,000			0.02	
25–VII	2,085,000	10,510	35% "	0.03	
26–VII	1,262,000			0.02	
27–VII	950,000	16,510	21% "	none	
28–VII	1,775,000			0.025	
29–VII	1,950,000	26,310	34% "	0.03	
30–VII	1,850,000			0.03	
31–VII	1,720,000	19,800	22% "	0.03	
1–VIII	1,480,000			0.035	
2–VIII	1,365,000	21,044	22% "	0.03	
3–VIII	1,500,000			0.03	
4–VIII	1,375,000	25,954	25% "	none	
5–VIII	1,475,000			0.03	Pyrodin by stomach tube.
7–VIII	2,100,000	14,354	38% "	0.03	Pyrodin by stomach tube.
8–VIII	2,230,000			0.04	Pyrodin by stomach tube.
9–VIII	2,125,000	30,250	25% "	0.04	Fresh solution of pyrodin.
10–VIII	1,415,000			0.04	Pyrodin by stomach tube.

Death during the night. Autopsy at 12.15 p. m. There was a small amount of clear, light yellow fluid in the peritoneum. Right lung showed moderate hypostasis and œdema. Otherwise the organs resembled in every particular those from rabbit I.

Microscopical examination.—The tissues from this rabbit, as well as those from the remaining animals, were all treated as in rabbit I, experiment A.

Bone marrow.—This resembles in all respects that seen in rabbit I. In the smears, however, there are a few nucleated red cells which may be classed as megaloblasts.

Spleen.—There is marked necrosis of the pulp and the Malpighian follicles are reduced in size. In places in the venous sinuses there are groups of mononuclear, non-granular cells like those in experiment A. In one group there were two megalokaryocytes and several phagocytes, and in one of the non-granular cells a mitotic figure was seen. Hæmosiderosis is marked. The erythrocytes throughout the spleen are for the most part shrunken and distorted. *Smears*, stained as in experiment A, show very many cells resembling lymphocytes with a moderate number of normoblasts and myelocytes which, however, seem less numerous than in rabbit I. There are many phagocytes and practically every red blood cell is distorted.

Liver.—There is marked fatty degeneration, affecting chiefly the cells of the central part of the lobule. There is no dilatation of the capillaries and no intracapillary nests of cells are to be seen. No megalokaryocytes are found. There is considerable hæmosiderosis. *Smears* show a few polymorphonuclear pseudoeosinophiles. Very rarely one finds a normoblast or a myelocyte; they seem to be about as numerous as they are in the heart's blood. Mastzellen are comparatively numerous. A few phagocytes are seen.

Kidneys.—Marked hæmosiderosis of the cortex; otherwise practically negative.

The remaining organs are negative.

The spleen, which has been active in this experiment as a hæmatopoietic organ, has assisted the bone marrow in the attempt to compensate for the anæmia, but there is no evidence of hæmatopoiesis in the liver.

Experiment C. Rabbit III. Male. Weight, 2170 grams. Pyrodin given by stomach tube.

Date. 1906	R. B. C.	W. B. C.	Hb.	Pyrodin	Remarks.
11–IV	5,050,000	9,020	53% (Miescher)	none	
18–IV	6,025,000	12,400	62% "	0.01	
19–IV	5,820,000			0.02	
23–IV	3,850,000	12,500	44% "	0.02	Rabbit seems lifeless.
24–IV	3,487,000			0.025	
25–IV	3,275,000	14,160	34% "	0.04	
26–IV	2,125,000			none	
27–IV	1,843,000			"	
28–IV	1,093,000	12,480	23% "	"	
30–IV	1,925,000	7,000	39% "	"	
1–V	3,441,000	8,600	47% "	0.03	
2–V	2,075,000	10,640	39% "	none	
3–V	3,721,000	9,280	51% "	"	Difficulty in passing tube.
4–V	3,833,000	5,600	51% "	"	Difficulty in passing tube.
5–V	4,087,000	6,932	58% "	0.035	
7–V	2,975,000	12,532	42% "	0.03	
8–V	2,750,000	13,120	33% "	0.035	
9–V	2,600,000	15,600	32% "	0.035	
10–V	2,450,000	26,800	25% "	0.04	
11–V	1,500,000	26,300	17% "	none	
12–V	1,400,000	20,400	19% "	0.025	
14–V	2,312,000	5,849	28% "	0.04	
15–V	2,300,000	6,620	26% "	0.04	Fresh solution of pyrodin.
16–V	1,993,000	19,520	23% "	0.04	
17–V	1,858,000	8,700	15% "	none	
18–V	1,730,000	7,464	16% "	"	
19–V	1,935,000	3,776	21% "	0.04	
21–V	2,566,000	4,088	28% "	0.045	
22–V	2,020,000	7,064	20% "	none	
23–V	2,012,000	17,600	22% "	0.04	
24–V	1,762,000	5,552	18% "	none	
25–V	1,525,000	8,900	17% "	"	
26–V	1,735,000	7,464	16% "	"	
28–V	2,225,000	3,700	28% "	0.045	
29–V	2,360,000	5,200	19% "	0.045	
30–V	1,880,000	16,800	15% "	none	
31–V	1,293,000	21,500	12% "	"	
1–VI	1,044,000	18,932	11% "	"	
2–VI	1,341,000	10,044	11% "	"	

Death occurred between 10 and 11 a. m. on June 4, 1906. Autopsy at 3 p. m.

There were small yellowish nodules in the liver, some of which had extended to the surface of the organ; they were slightly elevated, flat across the top, and rather firm in consistency. No areas of softening were found in them on section. In other respects the organs differed, macroscopically, in no essentials from those in the preceding rabbits.

MICROSCOPICAL EXAMINATION.—*Bone marrow.*—There is marked hyperplasia of the myeloid tissue, the granular marrow cells (myelocytes) being in the majority. The islands or cell-nests described by Bunting are well seen and many of the large non-granular cells in the center of the nests show karyokinetic figures. Phagocytes are present. In the *smears* there are many free pseudoeosinophilic granules; there are very few intact myelocytes.

Spleen.—This resembles the spleen in rabbits I and II in the decrease in size of the splenic follicles, the diminished number of cells in the pulp, and the presence of a few megalokaryocytes. Phagocytes are present in enormous numbers. A few pseudoeosinophile myelocytes are found in the pulp. In the venous sinuses and rarely in a capillary, collections of mononuclear cells resembling large lymphocytes are seen; at times a megalokaryocyte is present in these collections of mononuclear cells. Evidences of mitosis are not lacking in the cells collected in the venous sinuses. *Smears* show large numbers of nucleated reds, as many as six being found in one field (Leitz 1/12 oil immersion; ocular IV). The majority of the nucleated reds are normoblasts, though there are many intermediates and rarely a megaloblast (?). No definite cell division figures are found in the smears. There is a great number of lymphocyte-like cells resembling the non-granular, mononuclear cells of the bone marrow. A moderate number of pseudoeosinophile myelocytes is present. Mastzellen are very scarce.

Liver.—The liver cells show little change other than a moderate pigmentation of the cells of the peripheral zone of the lobules. In the liver capillaries, both in the central and peripheral zones, there are many pseudoeosinophile leucocytes, mostly polymorphonuclear with only an occasional mononuclear. Megalokaryocytes are not seen. Glisson's capsule is unaltered. The nodules found at autopsy present a central necrotic area surrounded by granulation tissue. *Smears* show many polymorphonuclear pseudoeosinophiles, very few normoblasts and mastzellen, few pseudoeosinophile myelocytes.

The remaining organs are negative except for pigmentation of the renal cortex.

Experiment D. Rabbit IV. Male. Weight, 2360 grams. Pyrodin given subcutaneously.

Date. 1906	R. B. C.	W. B. C.	Hb.	Pyrodin	Remarks.
12–IV	5,855,000	4,176	55% (Miescher)	none	
18–IV	5,662,000		59% "	0.01	
19–IV	5,860,000	6,800	59% "	0.015	
23–IV	5,612,000		51% "	0.015	
24–IV	4,820,000	5,200	44% "	0.03	
25–IV	5,170,000			0.04	
26–IV	3,125,000	8,844	43% "	0.03	
27–IV	1,664,000			none	
28–IV	1,406,000	6,920	11% "	"	
30–IV	1,440,000	2,800	17% "	"	
1–V	1,941,000	2,664	26% "	"	
2–V	3,360,000	2,488	39% "	0.03	
3–V	3,164,000	3,100	45% "	0.035	
4–V	2,714,000	4,700	43% "	0.03	
5–V	2,400,000	6,400	43% "	0.03	

Date. 1906	R. B. C.	W. B. C.	Hb.	Pyrodin	Remarks.
7–V	2,100,000	7,128	35% (Miescher)	0.03	
8–V	2,125,000	13,800	25% "	0.035	
9–V	1,662,000	18,080	15% "	none	
10–V	1,237,000	4,932	18% "	"	
11–V	1,807,000	5,376	24% "	0.025	
12–V	2,014,000	3,864	28% "	0.035	
14–V	1,468,000	4,480	22% "	0.03	
15–V	1,785,000	4,852	20% "	0.035	
16–V	1,262,000	11,200	15% "	none	
17–V	1,750,000	4,932	19% "	"	
18–V	2,160,000	2,640	24% "	0.035	
19–V	2,050,000	3,100	23% "	0.035	
21–V	1,281,000	3,360	12% "	none	Animal weak. Fur rough.

Animal died between 11 a. m. and 1 p. m. on May 22, 1906. Autopsy at 5 p. m. Large red clots in both ventricles and extending into the aorta; practically no fluid blood in any of the vessels or organs. The latter are macroscopically the same as in rabbit I. As in the preceding animals, no lymph glands or hæmolymph glands were found.

Microscopical examination.—*Bone marrow.*—The section shows marked hyperplasia of the bone marrow of the myeloblastic type. In the *smears* the myeloblasts are by far the most numerous, the erythroblasts and granular marrow cells being relatively few in number.

Spleen.—The alterations in the spleen resemble those seen in the three previous experiments, but they are less marked. Megalokaryocytes are present. *Smears* show, in addition to many lymphocyte-like cells, a few normoblasts and myelocytes.

Liver.—Sections show very little alteration. In the *smear* only two normoblasts were found after prolonged search, not more than smears from the blood showed, it seemed.

Kidneys.—Marked pigmentation of the convoluted tubules is found.

Lungs.—There is marked œdema and moderate congestion. In the capillaries one finds a few megalokaryocytes.

Experiment E. Rabbit V. Female. Weight, 1900 grams. Pyrodin given by stomach tube.

Date. 1906	R. B. C.	W. B. C.	Hb.	Pyrodin	Remarks.
16–X	5,500,000	8,200	61% (Miescher)	0.01	
17–X	5,500,000	8,240	62% "	0.02	
18–X	4,330,000	9,760	57% "	0.02	
19–X	4,310,000	6,240	48% "	0.035	
20–X	3,425,000			none	
22–X	2,055,000			"	
23–X	1,840,000	9,280	29% "	"	
24–X	2,105,000	7,200	39% "	"	
25–X	2,415,000	5,680	39% "	0.025	
26–X	2,880,000	7,760	40% "	0.035	
27–X	2,990,000	6,000	43% "	0.045	
29–X	2,410,000	7,360	34% "	0.045	
31–X	2,265,000	6,320	31% "	0.04	
1–XI	2,735,000	5,680	38% "	0.05	
2–XI	2,600,000	3,680	29% "	0.03	Fresh solution of pyrodin.
3–XI	2,510,000	6,160	26% "	0.04	
5–XI	2,585,000	17,840	29% "	0.04	
6–XI	2,310,000	5,600	30% "	0.04	
7–XI	2,660,000	5,520	35% (Miescher)	0.045	
8–XI	1,850,000	9,000	25% "	none	
9–XI	2,070,000	6,640	30% "	0.04	
10–XI	2,150,000	5,280	30% "	0.045	
12–XI	2,275,000	7,040	30% "	0.05	
13–XI	2,090,000	4,720	26% "	none	
14–XI	2,730,000	8,720	34% "	0.07	
15–XI	2,775,000	5,760	31% "	0.14	

Rabbit was found dead at 8 a. m. Autopsy at 11 a. m. Rigor mortis present. Spleen 8.5 x 1.5 x 0.5 cm. Right lobe of liver greatly atrophied. Two small nodules in liver and the normal mottling of the organ lost. Very small amount of slightly reddish ascitic fluid. Otherwise the findings at section were the same as in rabbit I.

Microscopical examination.—*Bone marrow.*—Both sections and smears show myeloblastic hyperplasia of the bone marrow.

Spleen.—The section resembles closely that from rabbit IV. A few pseudoeosinophile myelocytes are seen in the meshes of the pulp and there are a few megalokaryocytes. There are small nests of mononuclear, non-granular cells, which look like lymphocytes, in the venous sinuses. *Smears* of the spleen show many lymphocyte-like cells, rarely a nucleated red blood cell, and a few myelocytes.

Liver.—There is some cloudy swelling and pigmentation of the liver cells. No nests of cells are to be seen in the capillaries. The smears are negative.

Lungs show moderate œdema. There are no megalokaryocytes in the capillaries.

The other organs, excepting the kidneys which present the usual changes, are negative.

Experiment F. Rabbit VI. Female. Weight, (?)—average size. Pyrodin given by stomach tube.

Date. 1906	R. B. C.	W. B. C.	Hb.	Pyrodin	Remarks.
16–X	4,090,000	8,080	61% (Miescher)	0.01	
17–X	4,705,000	11,640	60% "	0.02	
18–X	4,025,000	8,640	52% "	0.02	
19–X	4,260,000	10,000	52% "	0.035	
20–X	3,590,000				Animal weak.
22–X	1,535,000			none	

At about 10 a. m. on October 23, 1906, rabbit died. Autopsy at 3.30 p. m. The organs were all negative except for marked anæmia. There was very little fluid blood. No bleeding on section of liver. Clotted blood in heart, arteries, and veins. Bone marrow grayish brown. Spleen 5 cm. long.

Microscopical examination.—*Bone marrow.*—The fatty marrow of the femur is largely replaced by cellular myeloid tissue in which there are a few normoblasts and a few myelocytes, the majority of the cells being non-granular mononuclears (myeloblasts). There are many megalokaryocytes and a few phagocytes. *Smears* reveal nothing additional.

Spleen.—The pulp is poor in cells. The capillaries and venous sinuses are greatly widened and filled with blood. The follicles are slightly diminished in size. There is a moderate

number of phagocytes. A few very small collections of mononuclear, non-granular cells are found in the venous sinuses. In the *smears* many cells resembling the myeloblasts of the marrow are present; there are very few myelocytes and no normoblasts seen.

Liver.—There is nothing unusual with the exception of a few giant cells in the liver capillaries. Smears show very few non-granular mononuclear cells like those seen in the spleen; no normoblasts or myelocytes are found.

Kidneys.—Slight cloudy swelling and pigmentation of the cortex.

Lungs.—An occasional megalokaryocytic embolus is to be seen.

No cause can be found for the rapidly progressive pernicious course of the anæmia in this case. The rabbit received exactly the same doses of pyrodin (and on the same days and hours) as rabbit V; in the one the blood count gradually fell till exitus lethalis occurred less than nine days after the beginning of the intoxication; in the other the fall in the number of the erythrocytes was less pronounced and a fatal issue did not result. The probable explanation would seem to be, in part at least, defective powers of hæmatogenesis in rabbit VI, such as one sees in the so-called aplastic pernicious anæmia in man. This assumption is further supported by the practical absence of nucleated red blood cells from the circulating blood during the entire course of the anæmia. In this case there was not, however, aplasia of the blood forming organs. It is true that there was not complete myeloid transformation of the fatty marrow of the femur, and evidence of hæmatopoiesis in the spleen, if present, was slight, but it is uncertain whether the hyperplasia of the blood forming organs in this instance is any less than that which might be found in the rabbit ordinarily after an acute anæmia lasting a litle more than eight days. No alterations, other than those characteristic of pyrodin poisoning, were found in any of the organs, and there is, therefore, a similarity between the result obtained in this experiment and certain cases of "aplastic" anæmia in man, for in the latter the disease process results, it seems probable, from excessive blood destruction with little or no evidence of compensatory blood formation.

The earliest attempt at studying hæmatopoiesis in anæmia of adult animals experimentally was made by Bizzozero and Salvioli (3) in 1881. After venesection in guinea-pigs and dogs they found large numbers of nucleated red blood cells in the spleen, which normally contains few, as well as in the bone marrow. In rabbits, whose spleen contains no nucleated reds normally in adult life, they were unable to produce changes similar to those obtained in guinea-pigs and dogs. They believed, as a result of their experiments, that the spleen was active in regenerating the blood. Later Gibson (4) repeated their experiments on dogs in part, with the same result, and he made the observation that many of the nucleated reds in the spleen presented division figures in the nuclei, a point strongly in favor of their local origin. In 1890 there appeared the work of Howell (5), in which he was able to show that, after severe and repeated bleedings, and in some instances after a single strong hæmorrhage, nucleated red blood corpuscles were demonstrable in the spleen of the cat with every indication that they were multiplying there, though normally these cells are not found in the cat's spleen in postnatal life.

In studying the spinal cord changes occurring in experimental anæmia of rabbits produced by pyrodin, von Voss (6) noted that there was a deposition of granular pigment in the spleen with areas of necrosis, fatty degeneration in the liver, and in the kidneys all stages of parenchymatous nephritis. Tallquist (7) directed his attention especially to the iron content of the organs of dogs, in which both acute and chronic anæmia had been produced by the administration of pyrodin and of pyrogallol, and was able to prove in many instances a marked increase in the iron of the liver with considerable deposition of hæmosiderin in the spleen, kidneys, and bone marrow frequently. In my own experiments there was a marked reaction for hæmosiderin in liver, spleen, and kidneys in rabbits I and II, the only ones in which it was tried, but the equally marked pigmentation of the cells in the remaining animals makes it probable that the same holds true in all six. In the bone marrow in my experiments the pigment is contained chiefly in phagocytes. In only one instance was fatty degeneration of the liver found, as von Voss reported, while in none of my animals were the renal changes sufficiently marked to consider the existence of a nephritis. Very recently Rothmann and Mosse (8) have studied the effect of chronic pyrodin poisoning in dogs and give additional results of the general findings at autopsy (Mosse). No changes were found in the lymph glands. The spleen, enlarged at autopsy as in the reports of all previous workers, contained much pigment and the follicles were entirely preserved; the characteristic pulp cells were not well preserved. The kidneys showed the usual changes, they say, in the epithelial cells of the straight and convoluted tubules. Hæmosiderosis of the liver was noted. Most interesting was the condition of the hyperplastic bone marrow, similar to that described by Reckzeh (9) in dogs after pyrogallol-anæmia. The cells often designated "Stammzellen" or myeloblasts were present in very large numbers, there were many normoblasts and few granular cells. Unlike others, Reckzeh described megaloblasts in addition to normoblasts in the bone marrow. The marrow of the femur in my experiments showed myeloblastic hyperplasia in all instances with the exception of rabbit III, in which there was a chronic infection, a fact which may explain the large numbers of granular cells.

Lastly, and of greatest interest in connection with the present work, Bunting (10) in 1906 showed, among other things, that chronic anæmia of rabbits, produced by the administration of saponin, lead in some instances to collections of cells in the venous sinuses of the spleen, just as Meyer and Heineke had found in man and as I found in my first two experiments.[8] "The peripheral venous sinuses of the spleen were much dilated and crowded with cells of the marrow type

[8] Mentioned in the preliminary report of Meyer and Heineke, 1905, q. v.

chiefly of the erythrogenetic series, but including many megalokaryocytes and leucocytes. The nucleated red blood cells were grouped much as in the marrow and showed numerous mitotic figures. The veins of other organs are practically free from nucleated red cells, except for an occasional small group in the liver and the constant presence of megalokaryocytic nuclei in the capillaries of the lung." In Bunting's rabbits the anæmia did not become very severe, and this he attributed to the vicarious blood formation occurring in the spleen. It seems much more likely, however, that in some way tolerance to the poison was established, for in my first experiment, where evidence exists of hæmatopoiesis in bone marrow, spleen, and liver as well, there developed, nevertheless, a profound anæmia with fatal issue. As in his animals, I have found megalokaryocytes in the capillaries of the lungs, but not constantly. They were not present in the liver capillaries in Bunting's experiments.

The anæmia produced by pyrodin is due, not to any interference with normal blood formation, so far as is known, but to a great increase in blood destruction. Pyrodin acts upon the red blood cells causing shrinkage and deformity and, as Heinz (11) has demonstrated, these effects are most pronounced about 24 hours after the administration of the drug. In my experimental animals the color index remained high, as in Tallquist's experiments. Fortunately in the present work, the complete blood examination was made always between 22 and 24 hours after the administration of the pyrodin. The changes in the red blood cells will be discussed in another paper. Suffice it for present purposes to say that the deformities in the red blood corpuscles which Heinz described occurred in all of my rabbits. The serum was examined several times for the presence of free hæmoglobin, but none was found, an experience similar to Tallquist's, where excessive doses were not employed. Study of the histological sections shows beyond a doubt, it seems, that the injured red blood corpuscles are taken up by phagocytes which are found in very large number in the spleen and in much smaller number in the liver and bone marrow. In a very short time all the injured cells are removed from the circulating blood, unless, possibly, a few recover and are able to functionate. This phagocytosis of red blood cells occurring in the spleen, liver, and bone marrow in experimental animals is of particular interest, since Warthin (12) has demonstrated a like occurrence in the spleen, lymph glands, hæmolymph glands, and bone marrow in pernicious anæmia in man. We have, then, produced experimentally an anæmia which may be, and probably is, like primary pernicious anæmia in its origin; in neither is there hæmoglobinæmia as a rule, though this may exist exceptionally, and in both injured red blood corpuscles are removed from the circulating blood by phagocytes found in the hæmatopoietic organs which possess the double function of forming and "cleaning" the blood.

In embryos Köllicker showed many years ago—and it is now generally accepted—that the liver is the chief and earliest hæmatopoietic organ. Later in fœtal life the spleen also assumes this function and finally the bone marrow becomes effective in blood formation. Toward the end of intrauterine life, and in the early part of post-natal life the liver and spleen cease forming blood, a function which is reserved solely for the bone marrow. As was noted before, Ehrlich has shown the similarity between the bone marrow of the embryo and that of many patients dying of pernicious anæmia. And Meyer and Heineke demonstrated a like analogy between the blood-forming liver and spleen of the embryo and the same organs in pernicious anæmia. They have also called attention recently to a further point of resemblance of embryo's blood with that seen in pernicious anæmia in the existence of a high color index in each and elsewhere I shall bring forward still another analogy in the presence of "Howell's nuclear particles" in the blood of the human embryo and in that of pernicious anæmia in man. It is evident, therefore, that the work of Meyer and Heineke has marked a distinct advance in the pathology of pernicious anæmia, in that they have shown, so far as it is capable of demonstration at present, that there is not a defective regeneration of the blood in pernicious anæmia (excepting aplastic anæmia), but rather a very great increase in blood formation, the spleen and, in some instances, the liver assuming this function.

In the present experiments it is not possible to prove absolutely that the liver and spleen have reverted to their embryonic condition and taken up the function of blood formation, but it is possible to say that they present the histological pictures seen in the liver and spleen of the rabbit's embryo during the stage of intrauterine life when it is believed that these organs are actively engaged in hæmatopoiesis, and the inference is, therefore, perfectly logical that their function is the same here as it is during fœtal life. That evidence of hæmatopoiesis exists in the spleen in practically all of my experiments and in the liver in only one instance may be explained by the fact that the spleen, which is the last to assume its blood-forming power, is the first to regain it, whereas the liver, beginning its hæmatogenetic function at an earlier period of intrauterine life than the spleen, re-assumes it with greater difficulty.

Conclusions.

1. The anæmia produced in rabbits by the administration of pyrodin (by stomach tube or subcutaneously) is one with a high color index and results from injury to certain of the red blood corpuscles which are then removed from the circulating blood by phagocytes in the spleen, bone marrow, and liver. This resembles the condition found in pernicious anæmia in man.

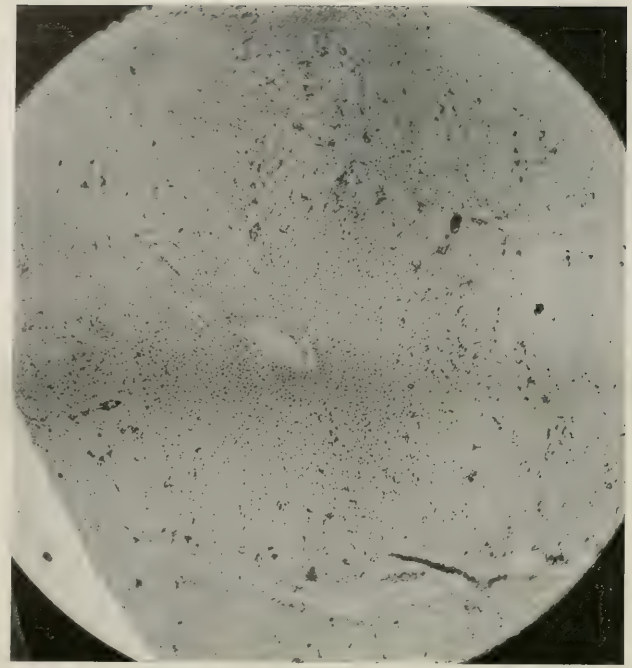
2. The increased blood destruction leads to increased (compensatory) blood formation.

3. The stimulus to increased regeneration of the blood, whatever its nature may be, leads to heightened activity of the hæmatopoietic function of the bone marrow, the occurrence of myeloid elements in the spleen and occasionally in the liver.

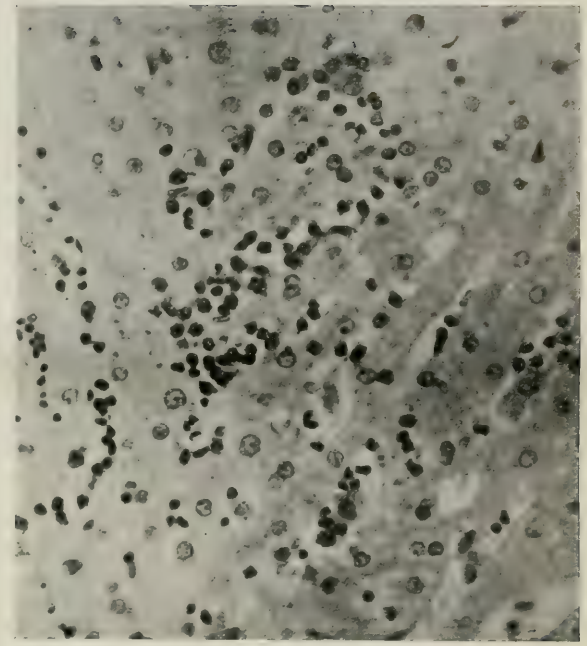
4. The changes occurring in the liver and spleen in the experimental animals are similar histologically, so far as the

1. Photo-micrograph of the bone marrow of rabbit I, experiment A, showing (myeloblastic) hyperplasia.

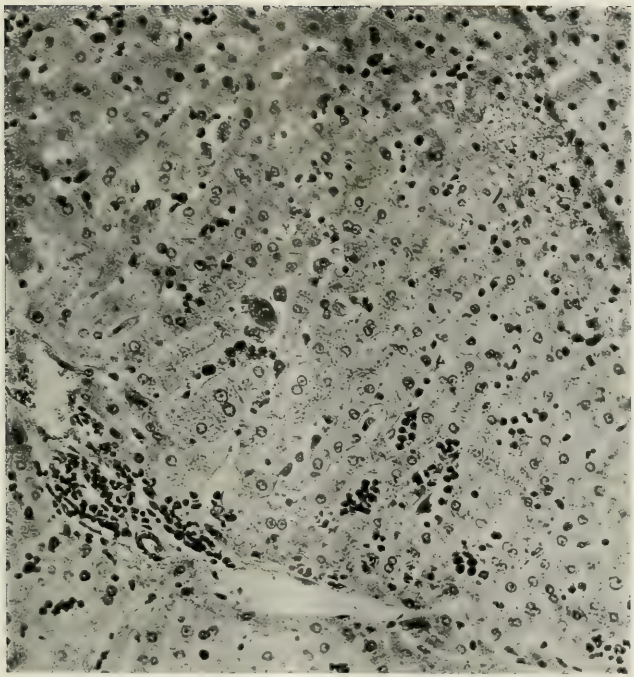
2. Photo-micrograph of the spleen of rabbit I, experiment A, showing (in the center) a venous sinus follicle with mononuclear cells having non-granular protoplasm.



3. Photo-micrograph of a liver lobule of Rabbit I, experiment A, showing the arrangement of the intracapillary nests of cells in the peripheral part of the lobule. (Low power.)



4. Photo-micrograph of the liver of rabbit I, experiment A, showing the intracapillary nests of mononuclear cells having non-granular protoplasm. (High magnification.)



5. Photo-micrograph of the liver of rabbit I, experiment A, showing several intracapillary nests of mononuclear cells and, in one of them, a megalokaryocyte. (High magnification.)

hæmatogenetic cells are concerned, to those seen in the normal rabbit's embryo at certain stages in its development, and it may be assumed, therefore, that the spleen and liver have taken up their embryonic function, *i. e.*, hæmatopoiesis.

5. The return of the embryonic function is in the reversed order of its disappearance.

6. Hæmosiderosis of the organs occurs as in pernicious anæmia of man.

7. The weight of experimental evidence favors the theory of increased blood destruction (the toxic theory) rather than that of decreased blood formation as the chief factor in the production of primary pernicious anæmia in man.

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MEASUREMENT OF THE COAGULATION TIME OF THE BLOOD, AND ITS APPLICATION.

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This work was undertaken in 1904, at Dr. Osler's suggestion, to test the value of Milian's new method of determining the coagulation time; and under Dr. Boggs' direction it was gradually broadened to include a comparative study of all the methods and their application.

A synopsis of the paper is as follows:

I. History of development.
II. General remarks.
III. Boggs modification of the Brodie-Russell instrument.
IV. A practical modification of Milian's slide method.
V. Coagulation times in pathological cases and calcium therapy.

Section I. History of Development.

A discussion of the development of this subject should naturally follow a chronological order. But this we do not propose to do. The development has been along three different lines, according to three different types of methods employed, as the following schema makes evident; and it shall be the key to our brief description.

I. Hayem's method.
  Slide methods.
    1. Testing with needle.
    2. Microscopical appearance of fibrin shreds.
    3. Watch glasses.
    4. Milian's method.
      Bezançon and Labbé's modification.
    5. Author's modification.
  Platinum loop method.
II. Capillary tubes:
  (a) Vierordt's methods.
  (b) Wright's methods.
III. Brodie and Russell method:
  (a) Pratt-Grützner modification.
  (b) Boggs modification.

Hayem (1) discusses the clinical value of a determina-

tion of the coagulability of blood and the deductions possible. His method consists in filling a flat-bottomed glass test-tube to a constant mark with blood as it flows from the wound. Time is counted from the issue of the blood from the vessels, and coagulation is completed when tipping the tube does not influence the shape of the clot. His results are very discordant. He could get nothing satisfactory, and says so. His times varied so in one and the same animal that he practically abandoned further observations he had planned. However, the method has been used by Dastre and Floresco (2) and by Brat (3), the latter much preferring it to Vierordt's or Wright's methods for accuracy. Brat states that the blood adheres to the test-tube walls in two minutes, and is immobile in three.

Bezançon and Labbé (4) describe Hayem's "éprouvette" more accurately. It is about 5 centimeters high, with an interior diameter of 7 mm., and is filled with blood to a height of 3 to 4 cm., being closed with a cotton tampon. The end-point is as Hayem described, but they make the method less accurate by recording as the beginning point, the moment when the first drop falls into the cylinder, instead of its appearance in the wound. They give 10 to 20 minutes as the normal coagulation time by this method.

The slide methods are classified with Hayem's, because the better of them depend upon the changes in the surface of the blood, or its contour, during movements of the slide, just as Hayem's does in the moving of the test-tube.

The simplest method (5) received the blood upon glass slides, and the consistency was tested from time to time with needles. When fibrin shreds were demonstrated in the gelatinous blood, coagulation had occurred. It is very evident no accurate work can be done with such crude technique.

An improvement (5) upon this was the study under the microscope for the first appearance of fibrin shreds. Schwab (6) recently revived this method. A small drop on a slide under a coverslip will show by the oil immersion a central zone of many layers of red blood cells and a peripheral ring, clear and fairly free from them. In the clear zone, the fibrin shreds are sought, and the time of their first appearance noted. He adds that the end point is often difficult to determine sharply, and the method is full of opportunities for gross errors. 5 to 6 minutes is the normal time.

Vierordt (7) mentions a method of which he made no use, however, simply testing it in the development of the method which now bears his name. It consisted in putting a drop of blood between two watch glasses. At first it is relatively fluid, flowing according to the movements of the glasses. The end-point is noted when the drop adheres to the glass.

In 1904, Milian completed a method of determining and recording the coagulation time of blood in capillary hæmorrhages, first suggested in 1901 (8). The clinical application was presented by René Jacquot (9). Using Hayem's test tube, Milian noted the difference in the coagulability of the blood at the beginning and at the end of a hæmorrhage. He then studied a hæmorrhage in detail. Taking as the beginning point the time the finger was pricked, he let the drops fall upon a series of numbered glass slides, noting the time the first drop was received and recording each successive drop,—also the time the last drop fell. "Coagulation of a drop is completed when one can tip the glass slide vertically without the drop upon it changing its shape, a moment easy to determine. When not coagulated, the drop takes the shape of a tear on moving the slide; but remains convex in outline when coagulated." Thus determined, the coagulation time of the first drop in a hæmorrhage of 41 drops was 17 minutes; of the last (41st), 15 minutes; of the 20th, as typical of the intermediates, 23 minutes 5 seconds. A drop obtained by pressure after the hæmorrhage had ceased, clotted in 6 minutes.

It was found constantly that the first and last drops of a capillary hæmorrhage coagulated more rapidly than the majority of the intermediates, and the last more quickly than the first. This he termed "coagulation dissociée" or "sur lame." For preserving these records, he devised a special chart (10), which is long and tedious, and which he himself soon discarded.

As completed (11), his technique is somewhat different

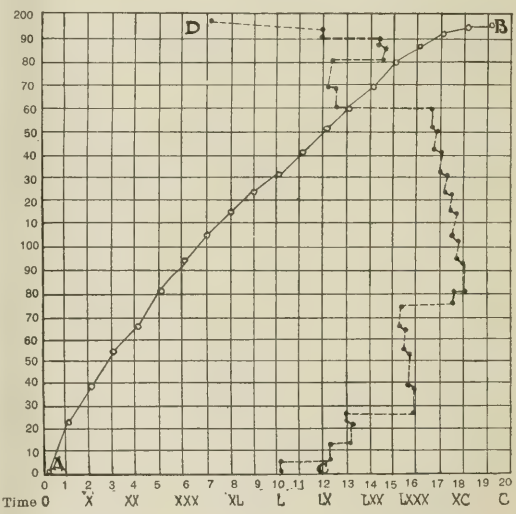

Fig. 1.—Milian's curves of coagulation and hæmorrhage.

from the original method. The blood is allowed to drop from the finger prick onto the slide, the slide not being touched to the drop as he had advised originally. The observations are to be made in as identical conditions of ventilation, temperature, and surroundings as possible. Coagulation has occurred when a uniform convexity in the contour of the drop is preserved on tilting the slide vertically. When the blood is still fluid, it sags to the lower side.

The results are recorded graphically upon a chart. The Curve of Hæmorrhage and the Curve of Coagulation are both plotted (see Fig. 1). For the curve of hæmorrhage (*A-B*)

the vertical divisions mark the minutes of the hæmorrhage, the horizontal ones the drops per minute. This shows the speed of flow.

In the curve of coagulation (*C-D*) the vertical divisions are in Roman numerals to indicate duration of coagulation in minutes. Here the curve of hæmorrhage shows 197 drops flowing in 19 minutes, at a rate of 23 for the first minute, 10 for the tenth minute, and 2 for the eighteenth. The curve is typical, approaching the horizontal more and more as the hæmorrhage is ceasing.

The curve of coagulation shows the first drop to clot in 51 minutes, the ninetieth in 90 minutes, and the hundred and ninety-seventh in 35 minutes.

In this method the recording chart has the advantage of giving considerable information about a capillary hæmorrhage in a brief, concise form. This we think a very important point. The more data given, the more inferences can be drawn. As his terms imply, this is a record of much more than the simple coagulation time of the blood. It pictures the powers of the local tissues in their defensive reaction. Of course, the duration of the hæmorrhage depends largely upon the depth of the puncture and the vascularity of the tissues. However Arthus (12), Delezenne (13), and Milian (14) have all shown that the influence of the skin is a vital factor —a most important point to bear in mind.

For comparative laboratory methods, this might be good; but the complexity and labor involved make it impracticable for bedside and ward work. A simpler method is more desirable. In the first place it requires, as a rule, much more than the customary puncture to obtain a hæmorrhage in which the blood will flow with such readiness as Milian's records show. The blood must drop from the finger. It is unusual to be able to get more than five or six drops by spontaneous flow from a wound with the lancet. From our experience, we believe an incision with a scalpel is necessary to obtain such records as 40 to 50 drops. We have found it difficult, even in this way, to obtain as many as 197 drops in what we could conscientiously call a capillary hæmorrhage and Milian (11) himself states that we must confine ourselves to capillary hæmorrhages alone in these practical observations.

The second objection is that there are so many drops which must be tipped up fairly often and their profiles studied, that it is a question if two observers can work fast enough together to catch the exact moment when each one of the drops is coagulated. When the end points begin to appear, it seems as if they all come at once. In one of our cases 28 drops reached their end points inside of 4½ minutes. The first drop to coagulate was the last received. 22 of the 28 drops were found clotted within a period of 2 minutes—so that accurate work was impossible. The limit of error is in direct ratio to the number of drops, and must be considered in a hæmorrhage such as is charted above.

Thirdly, the times obtained are less comparable to the action of blood in a wound than in any other method. It is hard to imagine a drop of blood spread out to about 1 cm. diameter on a glass slide remaining fluid from 60 to 90 minutes, as some of his records show. When a drop is received by letting it fall on the slide, as in this method, it varies from .6 to 1.25 cm. in diameter—about 1 cm. on the average. After coagulation has occurred, there is so much serum under the fibrin that the contour of the drop still changes on tipping the slide vertically. By waiting until this serum evaporates sufficiently to allow the contour to remain convex on moving the slide, one can obtain "coagulation times" of 60 and 90 minutes.

Bezançon and Labbé (4) describe a method evidently based upon Milian's. Three drops are allowed to fall upon three well-cleaned glass slides. Placed under a bell-jar, they are examined as in Milian's method, from time to time to determine the stage of coagulation. The fresh drop is convex upon the slide, but tends to flow towards the lower side in tilting the slide. As coagulation commences, the drop is deformed only slightly in the vertical position, and remains convex and immobile when the process is completed. The normal time by this method is about 10 minutes, 20 to 45 minutes being pathological. It differs from Milian's method in a lack of completeness in describing the characteristics of the hæmorrhage. Single drops cannot be compared when there is no uniformity of size. Furthermore, they make the error of counting time from the moment when the drop falls from the ear,—not when it appears in the wound. No records are quoted in detail.

The author's modification of Milian's method is described in detail in Section IV of this paper. It is practically the same as that recommended by Bezançon and Labbé but those details are carefully attended to which make it a reliable method for comparative results. The beginning point is the moment at which the blood appears in the wound. The end point is determined as by Milian. The drop is not allowed to fall upon the slide, but care is taken to always observe the same sized drop—4 mm. in diameter being adopted. A series of drops are picked up by touching a slide to the drops. The slide is placed upon a millimetre rule and those drops not wanted are wiped off. This can be made comparable to almost any other method by using a larger or smaller drop, according as the other method tends to have a longer or shorter average time. Detailed description and application follows in Section IV.

Mention[1] may be made here of a method in use in the Middle West, in which the blood is picked up in a series of platinum loops, and at intervals of one-quarter to one-half a minute, the loop is dipped in water. The coagulation time is taken at the moment when the blood ceases to be dissolved, but fibrin shreds are demonstrable and some elastic coagulum floats in the water.

Vierordt's (7) first suggestion for determining the coagulation time was extremely crude. When a capillary tube is touched to a drop of blood upon the skin, the blood will flow up the tube. By using a series of tubes and constantly

[1] A verbal communication.

testing, there comes a time when the developing coagulation prevents any more flow. He quickly saw the many possibilities for error in this method and gave it up. He then adopted the method which bears his name. He makes use of carefully cleaned capillary tubes 1 mm. in diameter and 5 cm. long. Touching the tip to a drop, the blood is allowed to flow up until a column 5 mm. long is obtained. Into these tubes is introduced a white horse hair about 10 cm. long. The hairs are previously extracted in alcohol and ether, and washed and dried, to make them as uniform in character as possible. Care must be taken not to handle that portion of the hair which is pushed through the blood, so as to project from the opposite end of the tube. The part of the hair projecting from the tube is not colored red by its passage through the fluid blood. The beginning of coagulation is noted when the fibrin separates and small coagula cling to the hair as it is drawn out. Coagulation is completed when no more new coagula are deposited on the hair. The hair which has been drawn out slowly, will now show a clear colorless portion at both its ends and a section between them covered with red coagula. The time is noted when the blood enters the tube. From this moment until the deposition of fibrin on the hair ceases, is the coagulation time. The average time of 262 observations upon himself was nine and a quarter minutes, with limits of seven and eleven minutes. This is very surprising when one considers the great amount of surface contact, but it is probable that the end point which he notes is a much more advanced stage in the coagulation process than that of other methods. He describes the finest details of obtaining the blood and the precautions to be observed to make the method as constant and the results as equal of comparison as possible. He uses the utmost pains to produce a method of value. He emphasizes such points as the need of obtaining a free flow at the puncture, the difference in drops when comparisons are made, the avoidance of dirt and pressure, the effect of temperature, currents of air, and contact. He realizes the many factors which cause variations, and is not overminute in the determination of the time, noting it only by quarters of a minute, so that small differences may be disregarded.

Vierordt deserves full credit as pioneer in this work of applying to clinical medicine the study of the coagulation time. His list of times in pathological cases was the first published, and his method of determination the first of any importance. It is interesting that this is the method used by Sahli (15) in his researches and the only one described in his textbook (16).

Wright's method with capillary tubes is probably the most widely known and most generally used of any. As first proposed (17), the apparatus consisted of six to twelve capillary tubes, calibrated to receive a blood column of 5 cm., with a diameter of about 25 mm. or 0.01 of an inch. A drop obtained in the usual way from the finger is aspirated into one of these tubes and the time noted when the tube is filled. The site of puncture is now wiped clean and "another drop of blood is pressed out for filling the next pipette." He fills at ¼ to ½ minute intervals. The stage of coagulation is tested by blowing down the tube at regular intervals. The results of testing are characterized as "liquid," "clotting," or "clotted." When the tube is found blocked, coagulation has occurred—"clotted." On the other hand, if the contents can be blown out upon a filter paper, demonstration of a shred of fibrin will distinguish "clotting" from "liquid."

For example:

Tube	1	tested	2	minutes	after filling	.....liquid.
"	2	"	3	"	" "	..... "
"	3	"	4	"	" "	..... "
"	4	"	5	"	" "	.....clotting.
"	5	"	4½	"	" "	.....liquid.
"	6	"	4¾	"	" "	..... "
"	7	"	5½	"	" "	.....clotted.
"	8	"	5¼	"	" "	..... "
"	9	"	5	"	" "	..... "
"	10	"	4⅝	"	" "	.....clotting.

So the coagulation time lies between 4 minutes 30 seconds and 5 minutes. The normal time is 2½ to 5 minutes, or rarely 6 minutes.

Wright emphasizes the importance for the accuracy of determinations, that the tubes be of the same size and the ligature about the finger be relaxed at frequent intervals. Six months later (18) he proposes as an improvement that the tubes be heated to 37° C. before filling and kept at that temperature during the process of coagulation. This is accomplished by placing the tubes and a thermometer in the pockets of a flannel bandage, which is fitted tightly about a tin cylinder containing water at the desired temperature. He also advises that the 5 cm. column of the blood be drawn up the tube a little way, in order that the blood should not come in contact with foreign substances at the tube's mouth.

Still later (19) in the same year the temperature was changed from 37°C. to 18.5°C., or half blood-heat for four reasons: 1. Coagulation is slower and therefore more accurate; 2, this approaches nearer to the ordinary ward temperature; 3, and so causes little, if any change in the temperature of the tubes; 4, it is the mean between the freezing point and blood-heat. In an article on the treatment of hæmorrhages and urticaria (20), the normal coagulation time observed at half-blood heat is stated to be 2 to 4 minutes in his standard tubes.

In 1897 (21) there comes another change in technique. To bring the tubes to a temperature of 18.5°C., they are immersed in a tumbler about two-thirds full of water of that temperature, with the butt ends downwards, fitted in India rubber caps. After filling them with blood, they are again immersed in the same water, but with points downward and without the caps, the column of air in the tube preventing the mixture of the water with the blood.

In 1902 (22), in an effort to make "more possible the advance in pathology and therapeutics along lines opened up by coagulo-metrical observations," Wright undertook to simplify the coagulometer, to reduce its cost to a minimum,

and so lead to its popularization. This he accomplished by constructing an instrument which can be made in the laboratory. The standard caliber, a tube 25 mm. in diameter, is approximated by constructing one of such caliber that 5 cu. mm. of mercury occupy a length of 5 cm. in the tube.

The calibration is ingeniously simple. A piece of ordinary glass tubing is drawn out into a fine and insensibly tapering capillary stem. Into the wide end of the tube 5 cu. mm. of mercury are introduced, this amount being measured off by means of a standard 5 cu. mm. pipette, such as is supplied with the Gowers hæmocytometer. Tilting the tube and moving the mercury along will show if there is a portion of the tube where the mercury column will occupy 5 cm. in length,—determined by comparison with a centimeter rule. The upper and lower limits of this are marked with a wax pencil. The mercury is displaced 1 or 2 cm. towards the wide end and these limits marked also, the tube being broken off at the lowest mark.

A series of such tubes are then made ready for use. Touched to a drop of blood, the tube is allowed to fill by capillary attraction until 5 cu. mm. have been obtained, as indicated by the marking. The tube, withdrawn from the blood, is then tilted so that the blood is between the two marks which delimit the portion of the tube of the standard caliber. The time of filling is noted as the beginning point. The tube is then placed point downward in water of the appropriate temperature. The series is tested as before, and the end point looked for is the first evidence of fibrin shreds in the blood when it is blown upon a filter paper. In normal blood this takes approximately 5 minutes.

Later in the same year (23), while applying the method to a study of typhoid thrombosis, a succession of slight pricks were used to obtain fresh blood for each tube, thus avoiding the use of a ligature or pressure and the influence of coagulation in the wound. And for the measurement of the standard volume of mercury, a special form of capillary pipette is devised.

Wright's latest modification has only recently been published (24), and can be understood best by reference to the original article. The method is practically the same, but the tubes are further improved upon. By means of his throttled capillary pipette, one is able to draw up just the right amount of blood with the greatest ease and accuracy. The water bath is used at 37°C., and the normal times reported varied from 1 minute 35 seconds to 2 minutes 10 seconds. This shortening of the time, however, is no improvement, rather a great objection. The almost unavoidable factors which cause variations are numerous, and there must be a limit of error wide enough to cover them. But when the coagulation time itself is but two minutes or under, too much importance may be laid on differences of seconds. The pathological differences and those dependent upon technique in this method are of about the same relative value, which must confuse the results.

The application of this latest method is shown in reports by Wright and Ross (25), Ross (26), Nias (27), and Fox (28).

The Brodie-Russell instrument, and the Pratt-Grützner and Boggs modifications are described fully in Section III. Suffice it to say here that, after a trial of all the methods mentioned, we have adopted Boggs's for our standard, as having the greatest accuracy combined with simplicity of technique.

SECTION II. GENERAL REMARKS.

Are deductions from results of experiments justified? What are we to infer from coagulation? its time, beginning and end point; its variability (daily), and other factors causing this?

It takes but little consideration of all the conditions present in the clotting of blood *in situ* (in the wound) to convince one that those same conditions can be imitated but partially in experiments. The question presents itself therefore, whether or not inferences from the coagulation time in experiments can be applied exactly to the same action of the blood in the body. We cannot say with certainty that when there is a delayed coagulation time a serious hæmorrhage will result, as for instance in an operation. But it has been shown repeatedly that it is difficult to arrest a hæmorrhage where the coagulation time is delayed; on the contrary, the time is short in the patients who bleed with difficulty. The coagulation time of a case of hæmophilia by the Boggs instrument was 16½ minutes, a greatly delayed time. A few hours later the clinical clerk found the greatest difficulty in arresting a hæmorrhage from a lancet and finally had to resort to bandaging the head with pressure on the ear. The hæmorrhage was not completely arrested until the following morning, 12 hours later. In this case, two capillary hæmorrhages from lancet pricks in the lobule of the same ear, on the same day, were arrested easily by contact with a cloth. The coagulation time observed on these two instances was 16½ minutes and 18½ minutes. This, as is evident, did not show definitely that any hæmorrhage would be serious,—and so the first two ear stabs failed to prove themselves; but the delayed coagulation time gave due warning of the possibility, as the third hæmorrhage made apparent. Many cases illustrate this same point. These show the relation between the coagulation in the wound and that *in vitro* to be not a fixed one. The conclusion, however, seems to be justifiable that, if the experimental coagulation time is within normal limits, the blood will clot in a wound with normal rapidity. At least there is no case to show that the blood clotted slowly and with difficulty when the time was not delayed. In the reverse case no sure prediction can be made, but a warning is at hand, which should be respected.

"Coagulation Time" must be accurately defined in order to make experimental times of comparative value. It is the period which elapses from the exit of the blood from the vessels until coagulation has occurred, measured by some one of the various instruments. It has never been applied to clotting in the wound. The time should be counted from the first appearance of the drop to be used, and not from the moment when it is picked off the ear, as is done by many

observers. This beginning point is a constant for all records, which is not the case in any other method of estimation, as the speed of flow of drops is variable. Thus from its constancy, it gives an exact coagulation time. For it is reasonable to suppose that the clotting process begins as soon as the blood appears on the surface of the skin or at the edge of the wound. From a deep puncture a drop large enough to be picked off will form in an instant, but from a superficial puncture or one in less vascularized tissues, the flow is slow and scanty. Coagulation proceeds while the drop is forming; and the added period of skin contact has a marked effect in hastening it. The longer a drop is in contact with the skin surface, the more rapidly it clots when transferred to the instrument. With a freely flowing drop the effect is minimal, and the beginning point is only shortened by a few seconds. But each second of skin contact added, shortens the coagulation time by minutes; *ex.*, L. G. had a coagulation time of 23½ minutes when there was a freely flowing hæmorrhage of 3½ minutes from a deep puncture. When the flow from a second puncture was scanty and lasted but 1 minute, the blood coagulated in 18¾ minutes. At another time: With free rapid flow, the time was 22 minutes; with comparatively slow flow, 15 minutes.

The end point must be more or less arbitrarily decided upon for the different instruments and methods. It should, of course, be clear and definite, always the same, and lend itself to satisfactory confirmation. No attempt was made to mark finer divisions of time than quarters of a minute, thus eliminating the small unavoidable variations as far as possible.

A marked characteristic of the coagulation time is its great variability, as is natural when its manifold factors are recalled. The size and character of the contact surface affects the liberation of the ferment. A drop received upon a vaselined or paraffined surface (29) will not clot at all. Uneven or dirty surfaces cause rapid clotting. With a contact surface of uniform character (glass), the greater its extent, the more rapidly coagulation occurs. This fact accounts largely for the variations in normal time secured by the different instruments. The time is shortest, about 2 minutes, in Wright's capillary tubes, because the amount of contact surface is greatest. For uniformity of character a smooth glass surface is used in all the instruments, whether it be capillary tube, disc, slide, or vessel.

Cleanliness of the skin and the instruments is of prime importance.

A word as to the part of the body from which blood is obtained. Hayem using his own method in simultaneous observations, found that the blood from the ear clotted in nine minutes and that from the thigh in two minutes. With a wide limit of possible error in Hayem's method it is none the less likely that the different character of the skin of the ear from that of the thigh would effect the coagulation time, as the more rough and scaly the skin, the faster is the normal clotting. The superficial blood supply also is not the same in ear and thigh.

It is not possible to make the character of the stab the same each time, but by trying always to obtain a ready flow one reduces to a minimum the factor of skin contact. A deep puncture will give the most uniform flow. Absolute equality of speed in successive hæmorrhages cannot be obtained, due to the difference in the vascularity of tissues of the same and different individuals, to changes in blood pressure, variations in vascular tone, dissimilarity of punctures, and many other inconstant and uncontrollable factors.

One should avoid producing active or passive congestion in any way. Tissue juices affect the time. The admixture of lymph and the increase in carbon dioxide both shorten it.

There is considerable difference in the coagulation time of the different drops of a hæmorrhage. Those at the beginning or the end clot more rapidly than those in the middle, because of the different rate of flow,—more evidence of the influence of skin contact. For this reason and because of the fact that often the flow is slow in starting, the routine is to wipe off the first drop which accumulates and use always the second or third for the experiment. In no case should those near the end of the hæmorrhage, be used.

From the first, observers have noticed the effect of temperature on coagulation. It is well known that cold delays and warmth hastens it. But it is only marked differences in temperature which affect the time, which, as a rule, are not met with in the wards or in the laboratory.

Drafts of air through evaporation, affect the coagulation time in those methods where the blood is directly exposed to them. The drop when the time is slow may dry up before it coagulates, if thus exposed.

Daily variation probably plays a rôle in the coagulation

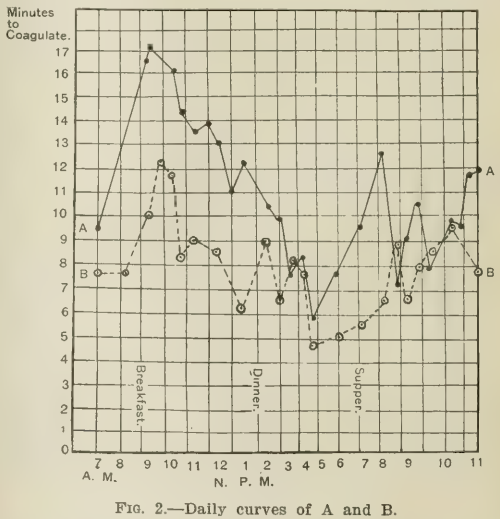

Fig. 2.—Daily curves of A and B.

time. Two curves were made, the authors taking observations every hour upon themselves with blood from the finger

tips. One used the Boggs modification of the Brodie-Russell instrument, and the other the practical modification of Milian's slide method (Section IV). To avoid influencing each other's results, they worked apart. Three interesting features of these studies may here be noted.

First, the fact is striking that their results correspond closely. The longest coagulation time for both A. and B. occurred at about 9 a. m., soon after breakfast. The fall from this was gradual until the shortest time during the day was reached at 4 p. m. After this the course for both was the same—a gradual rise.

The importance of the knowledge that such curves exist is evident. That they should exist and with some degree of constancy seems reasonable. The body activity, intake of food, digestion, sleep, and other physiological processes must have their effect on the body fluids, and they in turn on the coagulability of the blood. In a methodical life these influences would naturally be greater at definite periods of the day. Fuller discussion of these problems must be postponed until more records are at hand.

Second, the correspondence of the author's personal curves with the morning and afternoon observations in Table III, Section III, is noteworthy. These are the results of 251 observations made with the Boggs instrument. It is striking that of the morning records 67.5% were delayed times (beyond 8 minutes). The majority of the afternoon observations were normal times. This resemblance to the daily curves may be merely a coincidence, but it is strange that such a large majority of our cases of delayed times should occur in the early morning and the normal ones in the afternoon.

Third, even if there is no definite daily curve, it is evident that variations do occur during the day. For this reason, in a series of observations, it is important to make them at about the same hour.

As some drug the patient may be taking might alter the coagulation time, careful inquiry should be made as to this point, (see Section V), before drawing any results. The necessity of confirming the result cannot be too much emphasized. This can be done by wiping off the drop with a clean cloth or filter paper. When a definite coagulum is found the test is positive. In such cases only should the record be accepted.

Section III. Brodie-Russell Method, Boggs Modification.

Principle of the method; the original instrument; a modification by Pratt and Grützner; Boggs modification; relative merits of the three instruments; method of use in detail; the end point; normal time with the Boggs instrument; discussion of lack of uniformity in results of different observers; factors causing variation of particular significance for this method.

The principle on which the Brodie-Russell method of determining the coagulation time of blood is based is very simple. A drop of blood placed in a moist chamber can be set in movement by a very light draught of air tangentially directed. When coagulation has occurred, movement ceases. The process is watched under the low power of a microscope.

The original instrument was devised in 1897 by Russell and Brodie (30). It consists of a deep air chamber, closed below by a glass plate, upon which rests a layer of water. The air chamber is surrounded by a water-jacket, which has inflow and outflow tubes, so that the temperature of the air chamber can be regulated. Into the upper orifice of the air-chamber is fitted a metal ring in which is cemented an inverted truncated glass cone. The water jacket is pierced at one side by a glass tube, which is drawn out to a fine capillary at its inner end and is so directed as to throw a fine stream of air on the edge of the drop of blood.

Pratt (31), assisted by Professor Grützner of Tübingen, devised a modification of the original instrument in 1903. Pratt considered the water jacket and the truncated glass cone unnecessary features, which tended merely to make the instrument more complicated and costly. He omitted them in the construction of his modification without, as he thought, impairing the accuracy of the method. The Pratt-Grützner model is made by fastening a metal ring about 7/8 mm. in height and 1½ cm. in diameter to an ordinary glass slide by means of cement. A hole in this ring admits a small metal tube drawn out to a small orifice at its inner end, and to its outer end is attached a rubber bulb, as in the Brodie-Russell model. The upper free rim of the ring is coated with vaseline. A drop of blood is picked up on a heavy cover slip and the slip then placed on the ring, so that the drop hangs in the moist chamber. The vaseline holds it in place.

Boggs[2] devised an instrument in 1903, modelled after the Brodie-Russell. The water jacket is omitted as in the Pratt-Grützner type, but the inverted truncated glass cone is retained. The metal ring holding the cone has a milled edge, projecting slightly beyond the body of the instrument. (This is a decided advantage over the Brodie-Russell instrument, in which the ring is relatively small with a rounded edge which makes it awkward for handling.) The metal collar fits snugly in the upper opening of the air-chamber and is pierced by a small hole, which allows an equalization of pressure in the chamber when air is blown in by means of the rubber bulb. The metal air chamber is pierced at one side by a metal tube drawn out to a fine hole and adjusted, as in the Brodie-Russell method, so as to throw a fine stream of air at a tangent to the edge of the hanging drop. On opposite sides of the instrument are two metal bars, which are merely for convenience in handling.

Apparently there would seem to be very little choice in the use of any of these three instruments. They are all based on the same principle, as established by Russell and Brodie, namely, that the movement of blood in response to a draft ceases when coagulation has occurred. Practically, however, the Boggs model possesses decided advantages over the other two. It lacks the cumbersome and needless water-jacket of

[2] With his kind permission we are able to give the following description of it, which has not previously been published.

the original instrument, and its construction is altered in other ways so as to make it more practical. It is superior to the Pratt-Grützner instrument because of the retention of a cone, by which a drop of blood of approximately the same size is always observed. In the simple instrument of Pratt there can be no close uniformity in the size of the drop. This is a very serious objection, as there is a great and constant variation in the coagulation time depending upon this factor. The process is progressive and a small drop clots much sooner than a large one. The difference between drops 3 and 5 mm. in diameter is from two to four minutes for normal times, and this difference is increased in the case of delayed coagulation periods. This is well shown in records taken by the slide method, of which the following is one:

TABLE I.

	Slide method.		
Size of drop	3 mm.	4 mm.	5 mm.
Coagulation time	4′	5′	6′ 15″
" "	4′	6′ 30″	7′

This same variation is shown with instruments of the Brodie-Russell type, when the inferior surfaces of the cones have different diameters. The following are simultaneous records taken with three different instruments,—an original Brodie-Russell instrument, cone 3 mm. in diameter, and two instruments of the Boggs type, one with a cone surface of 3.5 mm., the other of 4 mm. in diameter. (No use was made of the water-jacket of the Brodie-Russell instrument.)

TABLE II.

	Brodie-Russell Instrument.	Boggs Instrumet.	
Size of drop	3 mm.	I. 3. 5 mm.	II. 4 mm.
Coagulation time	5′		9′
" "		5′ 30″	7′ 15″
" "		2′ 45″	5′ 15″
" "		9′	13′ 30″

The above tables, I and II, show definitely that the size of the drop is a very considerable factor in the length of the coagulation period. In the Pratt model no means are taken to make this factor constant. Its limit of error, therefore, is more than in the case of an instrument with a cone, which picks up a drop of uniform size. With cones of the same size, however, a series of successive observations upon the same individuals ought not to vary more than half a minute.

The technique in general is the same for all methods of determining blood coagulation, and has been fully discussed under General Remarks, Section II. The beginning point should be the first appearance of the blood from which a drop is to be taken for observation. The blood is allowed to well out at the puncture in the form of a small globule, and the inferior surface of the cone is touched lightly to it. The flat surface of the cone must be touched to the drop and care taken not to smear the edges of it. It is very simple to get a drop the exact size of the cone surface. When the glass is approached close enough, the blood seems to spring up and flow just to the edges of the disc. However, this will not occur upon a dirty cone surface. If the sides of the cone are smeared, or the drop fails to completely cover the cone surface, the latter must be carefully cleaned and dried. After the old drop is wiped off, time is taken on the first appearance of blood again, and another attempt made to pick off the right sized drop. It may be necessary to make a new puncture, as one should be careful not to use the late drops in a hæmorrhage.

With the drop on the cone, the latter is fitted quickly in the moist chamber. The apparatus is placed under the low power of a microscope and the motion of the blood caused by blowing with the rubber bulb is watched. As this is the most objectionable feature in the method, it should be made as uniform as possible for all records. Very light blowing, which is all that is required, at long intervals, minimizes the weakness of this method. Only the periphery of the drop need be watched. Here it is thinnest and clotting begins and ends first. Because of its thinness, the process can be better seen and the changes are more definite.

The changes in the movement of the red blood corpuscles set up by the blowing may, for the convenience of description, be divided into four stages:

1. Rotation of the drop as a whole or free flowing movement of the corpuscles individually. Fig. 3, *A*.

2. Cohesion of corpuscles and flowing movement in clumps and groups. Fig. 3, *B*.

3. Marked elasticity, flowing having ceased; a vibratory, elastic, *circular* motion. Fig. 3, *C*.

4. Elastic *radial* motion; indentation of the edge, the first appearance of which *radial* elasticity is the end point. Fig. 3, *D*.

Early in the process very light blowing starts the drop rotating as a whole, or causes a stream of corpuscles to flow about the periphery. The corpuscles move along individually and show no tendency to clump, Fig. 3, *A*. Gradually this movement presents a sticky, gelatinous appearance. The corpuscles begin to move in clumps and groups with clear, translucent spaces intervening, Fig. 3, *B*. In some cases a thin rim of corpuscles adhere along the periphery of the cone, probably the result of evaporation. This seems to have no particular influence on the end point, or the length of the coagulation period. Almost imperceptibly the drop takes on a definite elasticity. The flow of corpuscles becomes increasingly sluggish. Grouping and translucency disappear gradually and the corpuscles begin to move with a definite relation to each other. Elasticity becomes more and more marked, and flowing ceases completely. The corpuscles move in a *circular* direction when struck by the tangentially directed stream of air, but quickly recoil to their old positions. The movement is *circular* and elastic, Fig. 3, *C*. The drop should be carefully watched when this *circular* elasticity appears. In from 30 seconds to 7 to 8 minutes, as the time is short or delayed respectively, the final change occurs. This is marked by the appearance of a definite *radial* elastic movement. Different parts of the periphery should be watched, as this *radial* movement does not appear everywhere at once. *Circular* elasticity still persists, but the two are easily distinguishable. When

struck by the stream of air, the corpuscles, due to their *radial* elasticity, move as a gelatinous mass a little way towards the center of the drop, and quickly spring back into their old places. There may be at the same time a small indentation at the point where the corpuscles recede, which immediately fills in on the rebound, Fig. 3, *D*. The first appearance of this movement marks the end point in the determination. The time is taken at once, the cone of the instrument immediately removed, and an attempt made to pick off a clot from the cone surface with a cloth or piece of filter paper, as confirmation that coagulation has occurred. A firm visible clot can be picked off when *radial* elastic movement has been observed. Fig. 3, *E*, pictures a "vicious circle," which is merely a whipping of the blood from too vigorous pressure on the bulb, and here the end reaction fails to appear.

The end point is largely a matter of degree in the process of coagulation. The appearance of *radial* elastic movement does not indicate that the whole drop has clotted. It is merely one of the stages in the process; but it is of such definite and uniform occurrence as to form an almost ideal stage for observation, and for conformation a visible clot can be picked off where the definite elastic movement has occurred. In case there is no clot, a second observation should be made, as there may have been some error in judgment of the end point of the first record. In our studies, we have paid particular attention to this point of confirmation. In our early records the first appearance of the *circular* elastic movement was taken as the end point of coagulation. In no one of these cases could a confirmation be made by the presence of a clot. This stage forms a poor end point for other reasons. It is much more gradual in occurrence and is less definite, and allows greater variations in judgment. In some further observations, removal of the cone after the appearance of *circular* elasticity, but before *radial* movement had occurred, failed in most cases to show the least visible macroscopical clot. Such instances were most striking in the case of delayed times. This fact, therefore, that with the appearance of *radial* elasticity it is possible to demonstrate a macroscopic clot, is of importance, as it furnishes a constant technique, the results of which are strictly comparable.

Observers who have used the Brodie-Russell method have taken various portions of the different stages in the process as their end point. Pratt (31) took the moment when the individual movement of corpuscles ceased. He used no means of corroboration. Murphy and Gould (5) judged as an end point "the moment when the edge of the drop fails to rotate in response to the air current. As a control in all cases the cover glass was removed and the blood pricked with the point of a needle. Demonstration of fibrin shreds was regarded as a final evidence that coagulation had occurred." Brodie and Russell (30) considered the blood coagulated "as soon as a rim at the periphery is solid, and blowing simply indents this rim, without causing rotation." Pratt, Murphy and Gould probably used that stage which is labelled *C* in Fig. 3,—the *circular* elastic movement. Brodie and Russell very likely considered the *radial* elastic movement as the final change. This, with other considerations, may explain the inability of these different observers to secure a uniform average time.

It is only possible to approximate a normal time. The mean of a large series of records can be taken as the normal. Many individuals apparently in good health have delayed times. The majority of the records in a large series, taken on all sorts of cases, will be within normal limits. By tabulating such a series in columns of time divisions, it is possible to establish the limits for a normal time. The column summing up the greatest number of cases would reasonably be supposed to represent the mean normal time for the series. The average of the whole series of delayed, normal, and rapid times would be much higher than the limits established by such a table, and should not be considered as normal.

The following table was constructed from a series of 251 records, all taken with a Boggs instrument having a cone surface 4 mm. in diameter. Each record tabulated was confirmed by the presence of a macroscopic clot.

TABLE III.

Time of Day.	Time of coagulation in minutes.										Total.
	−3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11+	
A. M. 8-10....		1	3	3	4	4	4	7	5	15	46
" 10-12....	1	5	7	2	6	4	1	3	1	7	37
P. M. 12-2....		1	3		4	1	2	1		3	15
" 2-4....	2	2	4	6	2	2	3	2		4	27
" 4-6....	8	15	14	18	12	13	8	6	5	6	105
" 6+....		1	2	6	2	5	2		1	2	21
Total.....	11	25	33	35	30	29	20	19	12	37	251

163 of the records have times below 8 minutes, and, although more than half of the series are pathological cases, there are only 88, or 31%, with times above 8 minutes. The average time for the 251 records is about 9 minutes. But 37 of the records have a time of 11 minutes or above. The longest time in the series is 33 minutes. The mean of the 37 delayed times is 21 minutes, and this considerably raises the average for the whole series. Leaving them out, the remaining 214 records give an average of 6 minutes and 40 seconds. It is fair to conclude that records below 7 to 8 minutes are normal, while coagulation periods passing this limit are proportionally delayed.

The results of other observers are interesting. Pratt found an average time of 4 to 5 minutes. Murphy and Gould, from 300 observations, give an average time of 3 minutes 12 seconds, with limits of 3 to 6 minutes. Brodie and Russell's observations were made with reference to the influence of temperature and they publish only a few records. At 20°C., the average time on normal individuals was 7 to 8 minutes. Generally speaking, all agree that an average time for the Brodie-Russell instrument is between 3 and 8 minutes. The reasons for the differences are mainly two. In the first place, as has already been stated, all the observers have not used the same stage in the process as end point. Brodie and Russell, who used a late stage, record a much longer time. In the second place, it is very unlikely that all observers have

used the same sized drop. Again, the beginning point may have been different.

The general factors that influence the length of coagulation have been mentioned, but there are three that are of particular importance in the use of the Brodie and Russell method. These are, the size of the drop, the amount of blowing on the drop, and the stage in the process that shall be taken as the end point.

The question of the size of the drop is purely arbitrary, so long as neither extreme is used. The point of importance is that all instruments of this type should have uniform-sized cone surfaces. Records taken with instruments the size of whose cones vary, are valueless for comparison. There were three coagulometers in use at the Johns Hopkins Hospital. No two of them had cone surfaces of the same diameter. One was a Brodie-Russell instrument, and the other two were of the Boggs type. The diameters of the cone surfaces of the Boggs instruments were 3.5 and 4 mm. respectively, and of the other 3 mm. Table II shows the discrepancies in the results of simultaneous records by these three instruments. A 4 mm. drop is a good mean, and has been taken as the standard for our records.

The blowing on the drop is the one great objectionable feature of the method. This increases air contact, causes more rapid evaporation, and very likely has a considerable influence on the length of the period. If the factor were constant, the objection would be largely obviated. The observer can overcome this satisfactorily by using very light pressure on the bulb at long intervals. Continuous blowing should not be used, and the interrupted periods of blowing should be only momentary. The force of blowing can be easily judged by watching the drop.

The question of end point has already been discussed.

Section IV. A Practical Modification of Milian's Slide Method.

Reason for adoption of modification; size of drop the essential feature; selection of 3, 4, and 5 mm. sizes; change in contour on tilting; coagulation complete when no change in contour; confusion arising from presence of serum exudate; adoption of standard size drop; method of tabulation of records; time averages; comparison of results with Boggs method; delayed time and evaporation; normal time by slide method; practicability.

Having determined the inaccuracy of Milian's method, the following modification was tested.

Ordinary glass slides were used, though any glass surface will do. The ear was punctured in the usual way, the first drop wiped off and time counted from the appearance of the second drop. By lightly touching the under surface of a slide to this globule, drops of blood may be picked off for observation. The diameter of the drop picked off depends mainly upon the size of the globule on the ear. It is of advantage to hold the lobule of the ear out, so that the slide may be horizontal when touched to the drop. The drops being upon the under side of the slide, it is turned quickly to prevent them from flowing. Placed over a scale, those drops of the required size are chosen and the rest wiped off. Coagulation is judged as by Milian's method. It is complete when tilting the slide will cause no change in the contour of the drop.

The size of the drop is the essential feature of this modification. Milian allowed the blood to drip from a puncture wound upon the surface of a slide, and the drops were usually about 1 cm. in diameter. The size of the drop obtained by touching a slide to a globule can easily be controlled. Usually three to four drops were picked off on one slide, and as a rule two to three slides were used. When the drops were measured on a millimeter scale, only those approximating 3, 4, 5, and 6 mms. in diameter were saved for observation. The others were wiped off to avoid confusion. Where so many drops are used, it is necessary that time be taken on the first appearance of each new globule on the ear. So there are usually two or three different beginning points for the records and the slides should be numbered or kept in the order of these beginning points. Particular care was taken in all our records to have one 4 mm. drop for comparison. A number of simultaneous observations were made too with the cover-slip hanging drop method.

There are two ways of watching these drops to determine when coagulation has occurred. The contour of the drop may be watched from the side. In this case the appearance before coagulation will be as shown in Fig. 4, *A*, and after coagulation, as in Fig. 4, *B*.

Another way is to hold the slide to transmitted light and judge if there is a flow in the drop by the changes in density. The denser portion is in the center when coagulation has occurred, and at the lower edge according as the slide is tilted, when the drop is still fluid. Fig. 5, *A* and *B*.

It is well to combine these two methods as an aid in judgment of the end point. As a rule it is easy to judge when coagulation has progressed far enough to prevent a change in the contour on tilting the slide. Each observation should be confirmed by picking up a macroscopic clot with the tip of a cloth or filter paper.

The 4 and 5 mm. drops are the best adapted for this method. In the smaller ones the contour changes are difficult to judge, and the larger ones meet with the same objections, as in Milian's method. The 4 mm. drop gives a definite end point, except for very long times. In delayed times, evaporation is such an important factor that the 5 mm. size gives more satisfactory results. The 4 mm. drop may be so nearly dried up as to prevent the judgment of an end point. It is well, therefore, to always get a 4 and a 5 mm. drop for observation.

Tables IV and V are made from simultaneous records with the Boggs and slide methods. In the first table all four sizes of drops were observed; in the second, only the 4 and 5 mm.

TABLE IV.

	Slide Method.					Boggs Method.
					Average.	
Size of drop	3 mm.	4 mm.	5 mm.	6 mm.	4–5	4 mm.
Time in minutes	3½	4¼	6	8¼	5½	5½
" " "	4½	7	9	12½	8	7¼
" " "	9¼	11½	13¾	17½	13	

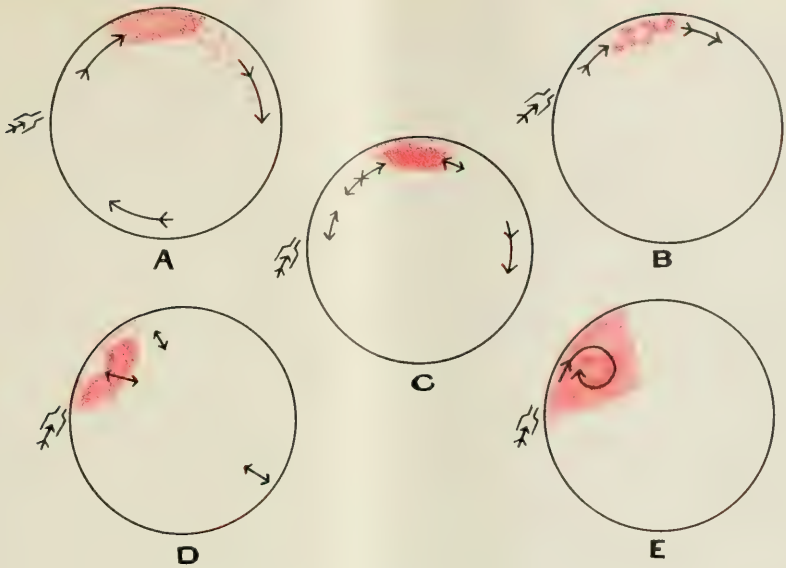

FIG. 3.—Stages in the coagulation process as seen under the microscope.

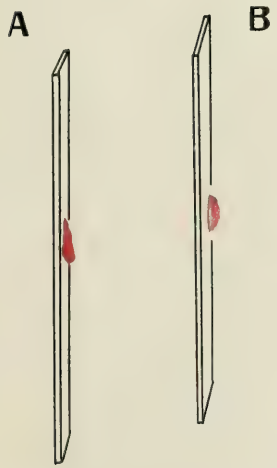

FIG. 4.—Contour of the drop before and after coagulation.

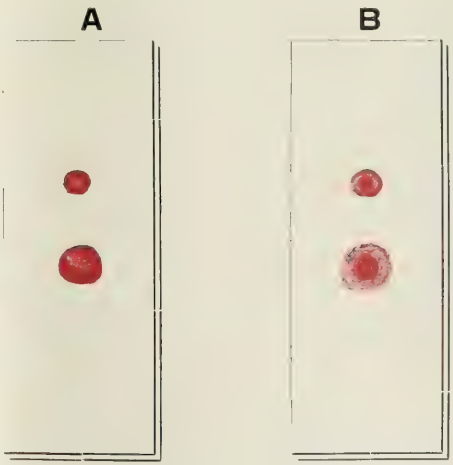

FIG. 5.—Same by transmitted light.

TABLE V.

	Slide Method.			Boggs Method.
Size of drop	4 mm.	5 mm.	Average 4–½	4 mm.
Time in minutes	6	8¼	7½	7
" " "	6¼	8½	7¼	6¾
" " "	6½	9½	8	8
" " "	5½	9½	7½	9
" " "	6¾	8¾	7½	8
" " "	6½	8	7¼	8
" " "	5¾	9½	7½	8¼
" " "	5¼	6¼	5¾	6

From the above two tables it is seen that the averages correspond very closely to the times obtained with the Boggs instrument. The time by the Boggs method seems to range between that of the 4 mm. and 5 mm. sizes of the slide. The 4 mm. drop upon the slide is exposed and naturally clots more rapidly than the 4 mm. drop protected in the moist chamber of the Boggs instrument. But a 5 mm. drop coagulates more slowly. So 4 mm. and 5 mm. drops are taken, and the mean of their coagulation times is what we term the *time average.* This lends itself most favorably to comparison with the results of the Boggs instrument.

The slide method as a quick, convenient and practical means of determining the coagulability of the blood is thoroughly reliable, and can be used in the laboratory or sick room. Its simplicity is the greatest point in its favor. The fact that the whole apparatus is but a clean glass slide and a millimeter scale permits everyone to use it.

The chief objection is the exposure and consequent evaporation. This apparently has little effect on the result in those cases where the time is within normal limits, and is no more objectionable than the blowing in the case of Brodie and Russell's method. But where the time is very much delayed, evaporation has so much better chance to modify the result that this is very often unsatisfactory. Besides the evaporation, the mechanical tilting hastens the time.

The records in the following table show that the method is of practical value even in delayed times.

TABLE VI.

	Slide Method.			Boggs Method.
Size of drop	4 mm.	5 mm.	Average 4–½	4 mm.
Time in minutes	8	9½	8¾	11½
" " "	7¾	8¼	8	11¾
" " "	7½	10¾	9	12
" " "	...	(1) 12½	...	12
" " "	...	(2) 10¾	...	....
" " "	13	15¾	14	14
" " "	13	...	...	15½
" " "	14½	15¼	14¾	14½

The average time for the slide method, taking the mean of the 4 and 5 mm. drops as the record for a case, is practically the same as that for the Boggs instrument with a cone surface of 4 mm. The great majority of the records fall between 5 and 8 minutes. Anything above 7 to 8 minutes is delayed. Below 8 minutes a record would be within the limits for a normal coagulation time.

In an attempt to determine the time significance of evaporation as a factor in the coagulation process, the following modification of the simple slide method was resorted to. Hanging drop slides used in bacteriological work were smeared with vaseline about the rim of the well. The blood for observations was then picked off on ordinary cover slips and these placed over the well, so that the drop would be in a closed chamber. The vaseline holds the slip in place, prevents its moving when tilting the slide, and seals the chamber. The end point for the drop was determined in the same way as for the plain slide. Judgment of this was, however, somewhat more difficult, as the contour could not be seen so clearly and the determination had to depend almost wholly on density changes, as shown in Fig. 5, *A* and *B*. In each case simultaneous records were taken by Boggs' instrument and by the slide method.

The results may be briefly tabulated as follows:

TABLE VIII.

Boggs Method.	Slide Method.			Cover-slip Method.		
4 mm.	4 mm.	5 mm.	Average.	4 mm.	5 mm.	Average.
11½	8	9½	8¾	11¾	....	....
7¾	5½	6½	6	7¾	....	....
6	4¾	6½	5½	6	....	....
7¼	8¼	10	9	9	....	....
8	6½	9½	8	9	....	....
10¼	8¾	10	9¼	9¼	....	....
8¼	5½	6½	6	9	10½	9¾
8¼	6¾	...	...	8¼	....	....
9¾	...	10	...	...	12	....

It is seen from the above table that evaporation, or open exposure, is a factor of considerable importance in hastening coagulation. The times in the 4 mm. column of the cover-slip series correspond more closely to the records of the 4 mm. drops of Boggs method than do the figures in the 4 mm. column of the slide method. As a rule they tend to be longer than the Boggs records, and this is probably due to the fact that the blowing on the drop, by the Brodie-Russell scheme, exerts an influence on the clotting period that is not present in the cover slip. Each have closed chambers, but the end points are very unlikely to correspond exactly, as the methods of determination are so different. It is fair to assume, therefore, that the difference in the times of the 4 mm. drops for the two slide methods is very largely due to the more rapid evaporation in the case of the unprotected drop. The difference is slight, and inasmuch as the simple slide is so much more convenient, the cover-slip method was used merely to demonstrate the point in regard to evaporation.

Section V. Coagulation Times in Pathological Cases, and Calcium Therapy.

I. Pathological cases, icterus; typhoid fever; urticaria; purpura; hæmorrhages; anæmias; aneurisms.

We have considered:

(a) Catarrhal jaundice.
(b) Jaundice due to cholelithiasis.
(c) Jaundice due to malignant disease.

The cases of catarrhal jaundice have shown a normal coagulation time, 5½ to 6 minutes. (All the records are taken with the Boggs instrument.) In jaundice due to cholelithiasis, the times range from 5½ to 12½ minutes, with an average of 8 minutes. This is on the upper limits of normal and is in contrast to jaundice due to malignant disease, where the average is 13¼ minutes, and the limits 9 to 20½ minutes.

For typhoid fever Wright (32) has claimed a delayed time during the acute stage and a short time in convalescence, and he lays stress upon the occurrence of hæmorrhage and thrombosis in connection with this. Our cases have shown the difference, but it has not been marked. In contrast to an average of 7 minutes in convalescence is that of 9 minutes in the acute stage. Some individual cases have been more striking:

L. C.—12th day, 12 minutes; 23d day, 7½ minutes; 31st day, 3 minutes.

J. L.—15th day, 13¼ minutes; 21st day, 9¼ minutes; 44th day, 5¼ minutes.

None of the cases with hæmorrhage have had a delayed time, and all of them have shown an increased coagulability after the hæmorrhage.

In the typhoid thromboses, the longest time was 6½ minutes, the average 5½ minutes. The majority of our cases have been on a milk-albumin diet, and the few fed more liberally showed no differences from the general group.

Four cases of hæmophilia had times ranging from 11 minutes to 33 minutes. Two of them were brought down to 5 and 6 minutes with calcium:

J.—12 minutes, 6 minutes after calcium.

Dr. B's Case.—30 minutes, 5 minutes after calcium.

The times in urticaria have been variable. Some have been as delayed as 9½ minutes. Some of the cases with diminished coagulability are greatly benefited by calcium. Cases of purpura, hæmaturia without known cause, epistaxis and various hæmorrhages more profuse than usual, have shown times varying from 6 to 9¼ minutes. In this class calcium is of great help.

In the primary anæmias no markedly delayed time has been found. One case of pernicious anæmia had a time of 9½ minutes. The majority range from 4½ to 7½ minutes. We have observed no case of leukæmia with hæmorrhage. An acute lymphatic leukæmia without hæmorrhages had a time of 8¼ minutes. The blood in two very severe secondary anæmias,—a case of hæmaturia and of typhoid fever respectively,—clotted in 14¾ and 14 minutes. As a rule they were not different from the primary cases.

Finally, we have observed many aneurism cases, with the idea of increasing the coagulability of the blood. Never have we found them to have delayed times.

II. Calcium therapy; in cases of normal coagulation times; in those of delayed times; form of calcium; loss of effect after too long administration. Will calcium cause a delayed time? Course of increasing doses. Action of citrates; how to give them; effect of calcium plus citrates.

Calcium therapy.—Calcium therapy in relation to the coagulation of blood is a subject of growing importance and interest. It is generally well known that calcium salts given by mouth, per rectum, subcutaneously, or intravenously, tend to shorten a delayed coagulation time; but the fact that the effect of any dose wears off after continued administration is not so well known, nor is it understood how a delayed time may be reduced and maintained as such. It is too frequently the case that calcium is ordered to assist in the control of a hæmorrhage, when no attention at all has been paid to the coagulation time. The first requisite is always a determination of the time. A normal time is not a contraindication to calcium in all cases. The increased calcium content of the blood may be of aid even when the time is normal. We have found that a normal time can be further shortened. For instance:

H. S.—Aneurism, 7½ minutes; 3 minutes after calcium.

L. N.—Aneurism, 5½ minutes; 3¼ minutes after calcium. Same case again, 7 minutes; 4 minutes after calcium.

However, it may do harm in some cases. Take for example a case of intestinal hæmorrhage in typhoid fever. The bleeding is due to the erosion of a vessel, and it has never been our experience to find a delayed coagulation time in these cases. In addition a hæmorrhage of considerable size will in itself shorten the time. And yet, with great regularity, one finds calcium ordered after the hæmorrhage, often the only thing the patient is getting by mouth. Whether too much calcium causes thrombosis or not, as Wright claims, there appears to be at least a possibility of this.

Having found the time delayed, calcium is indicated. The lactate is the best salt, as Boggs (33) first pointed out. The chloride is too irritating. We have never seen the lactate cause the slightest gastric disturbance. A good way to give it is in suspension in simple syrup, or the powder or capsules may be used. A solution of the chloride in normal salt may be used for infusion intraperitoneally or intravenously, but subcutaneously it may cause great sloughing. One of our cases was complicated by a breast abscess with calcification (34). It has been suggested that the lactate is split in the stomach and the calcium absorbed as a chloride. If so, the best time for the administration would be after meals. Wright has claimed that too much calcium will lengthen the coagulation time, more even than it was previously. Our experience has been as a rule that when one does continue it too long, the effect wears off and the time returns to about what it had been previously. We have but one case in which possibly the calcium itself lengthened the coagulation time to more than it had been before it was started. It is:

S.—Malignant Jaundice.

Coagulation time.	Date.	Calcium lactate.
9¼ minutes in a. m.	Apr. 13	
	Apr. 14	gr. 80 q. d. begun.
	Apr. 15	continued.
	Apr. 16	gr. 120 q. d.
	Apr. 17	gr. 160 q. d.
8 minutes in a. m.	Apr. 18	continued.
	Apr. 19	gr. 240 q. d.

Coagulation time.	Date.	Calcium lactate.
17 minutes in p. m.	Apr. 20	gr. 480 q. d.
20½ minutes in p. m.	Apr. 21	Calcium discontinued.
	Apr. 22	
11¼ minutes in a. m.	Apr. 26	gr. 10 at 8-12-4-8.
7½ minutes in p. m.	Apr. 26	
6¾ minutes in p. m.	Apr. 28	

Our idea is that in the gap of four days without a record, the coagulability was increased to normal, and was then delayed again by too much calcium. As the progressive increase in calcium kept up, the time became more and more delayed. When the intake stopped, the time became shorter, as the body rid itself of the excess calcium. Later, the time was reduced to normal by a small dose of calcium lactate.

As a rule, however, the type of cases is as follows:

M. H.—Jaundice. Cholelithiasis. Was receiving calcium lactate gr. 80 q. d. before first observation.

5½ minutes in p. m.	1st day.	
4½ " "	2d day	
8 " "	4th day	increased to gr. 120 q. d.
7½ " "	5th day	
5½ " "	6th day	
6 " "	7th day	
9 " "	8th day	

F.—Aneurism. Calcium was given to increase the coagulability and induce clotting.

5½ minutes....	1st day	Calcium lactate gr. 45. q. d.
3½ "	2d day	
3¼ "	3d day	
7 "	5th day	Calcium increased to gr. 90.
4 "	7th day	
7 "	11th day	

A. S.—Jaundice. Cholelithiasis.

9½ m. before Calcium.
6¼ m. on 2d day of Calcium.
4 m. on 4th day of Calcium.

I. B.—Malignant Jaundice.

11 minutes............	calcium.
9 "	
19 "	increased calcium.
14 "	
9 "	

These typical cases show how the calcium increases the coagulability, but can maintain it only about three to five days. If the dosage is then increased, the time is again shortened.

In order to reduce a delayed coagulation time and maintain it as such, it is better to begin with a small dose, as gr. 10, four times during the day. Daily determinations are made, and when the time is becoming delayed again, increase the dose to gr. 20 q. 4 h., then to gr. 30 and gr. 40. As a rule, the small increases will fall due every 3 to 5 days, and will succeed in maintaining a short coagulation time. Large amounts of the drug are inconvenient to take. So we usually go no higher than gr. 40 q. h. After a free period of 3 to 5 days, the effect is gained as before, in beginning a new course. This fact suggested a second method of giving a small dose for 3 to 5 days and following with a free period of the same length, thus alternating as long as necessary.

In contrast, the citrates are supposed to have the opposite effect, namely, to delay a short coagulation time. Our experience is limited, as we found very few cases where a delayed time was desirable. It would seem, however, that their effect wears off in a manner analogous to that of calcium; that to maintain a delayed time, there must be small increases in the dose at intervals.

The question arose as to whether the citrates might neutralize the effect of the calcium if given at the same time. L. G. was receiving potassium acetate and citrate gr. 15 q. 4 h. as a diuretic. On the third day she had an epistaxis of 400 cc. Calcium lactate was given, gr. 15 q. 4 h., and increased to gr. 30 on the seventh day. Both were continued for 9 days, during which time the coagulability of the blood remained diminished. Times of 10, 10¼, 9¼, and 8½ minutes were obtained. The first normal time, 7 minutes, was on the day after the citrates were discontinued. The evidence in this one case points to the citrates acting as a check upon the calcium.

We then made use of a case of erythema nodosum, as an experiment in this line. The chart explains itself.

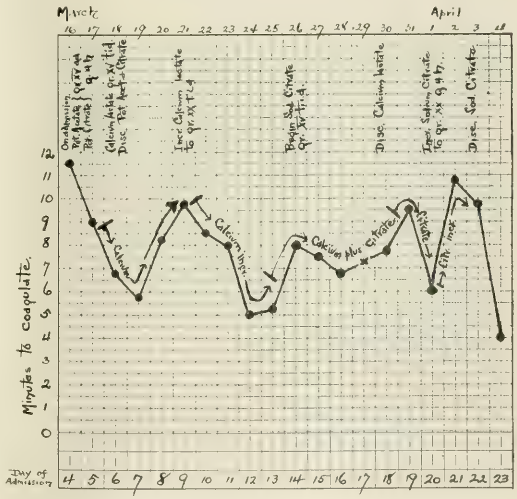

FIG. 6.—A. G. Erythema nodosum.

The delayed time was reduced with calcium; its effect wore off, and it was a second time reduced. Then with a time of 5¼ minutes the citrate was begun. For five days the two together maintained a fairly constant time between 7 and 8 minutes, which is about a mean between the extreme effect of the calcium, 5 minutes, and that of the citrate alone, 10¾

minutes. Then with the citrate alone, its effect soon wore off, but was renewed by an increase in the size of the dose.

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ON WRIGHT'S METHOD OF MEASURING THE ALKALINITY OF THE BLOOD.

A PRELIMINARY NOTE.

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In the course of certain investigations on methods of measuring the alkalinity of the blood now being pursued in this laboratory under the direction of Dr. Thomas R. Boggs,[1] we have had occasion to test the value of the method described by Sir A. E. Wright (1); and we have considered it of interest to give a preliminary report of our results, discussing only the practical technical value of the method, and not attempting, for the present, to deal with the more complex chemical questions involved.

The method as described is as follows: Blood is drawn from a finger into a capsule, one or both ends of which are sealed. It is then allowed to stand for from 3 to 24 hours. This is done, because, as shown by Zuntz (2), Peiper (3), and Winternitz (4), the alkalinity of the blood diminishes rapidly until coagulation occurs, after which it remains fixed. When the blood has stood until a condition of constant alkalinity is reached, it is titrated. The capsule may, however, first be centrifugalized to further separate the serum from the clot. The titration is by means of capillary pipettes like those used in the opsonin work. Solutions of normal sulphuric acid, diluted 20-, 30-, 40-, 50-, and 60-fold are prepared. The titration is against delicate red litmus paper, prepared by acidifying very fine (Grübler) neutral litmus paper in a solution of 1:20,000 hydrochloric acid, repeatedly washing with distilled water, and then drying in an oven at 120° C. Such paper should show an alkaline reaction to normal blood serum diluted forty times. The paper should be glazed or made as smooth as possible by rubbing with a glass rod.

The acids and indicator being ready, a pencil mark is made about 2 cm. from the end of the pipette to be used. Serum is drawn from the capsule into the pipette almost up to the blue mark, leaving an air-bubble index. Then an equal volume of $\frac{N}{20}$ sulphuric acid is sucked in, and the serum and acid are mixed by blowing them into a watch glass and reaspirating. A drop of the mixture is then put on a strip of the litmus paper. If this is still acid, the same procedure is instituted with equal volumes of serum and of $\frac{N}{30}$ sulphuric acid, and so continued down with $\frac{N}{40}$ acid, etc., until the mixture shows an alkaline reaction. When this is obtained, say with equal volumes of serum and $\frac{N}{40}$ acid, an intermediary solution of $\frac{N}{35}$ acid is made from equal volumes of $\frac{N}{30}$ and $\frac{N}{40}$ acid and the titration is repeated with this dilution. The acid dilution first neutralizing the serum is considered as the measure of the alkalinity, and the alkalinity is expressed in fractions of normal acid; for example $\frac{N}{35}$, $\frac{N}{40}$, etc. No attempt is made to titrate with acids varying by less than a five-fold dilution. Wright found that in a series of 13 normal persons the serum possessed an alkalinity varying from $\frac{N}{30}$ to $\frac{N}{45}$, or an average of $\frac{N}{35}$. In the author's words, this means that the "alkalinity of blood under ordinary conditions of health is such that the addition of one volume of a normal acid, 35 times diluted, to an equal volume of serum, just suffices to deprive that serum of its power of blueing sensitive litmus paper."

Wright advocated this method, not as an accurate measure of the nature or amount of the substances producing the alkaline reaction, but as a convenient approximate estimate of the total alkalinity of the circulating blood. In using *serum* we obviously only make a partial calculation of the total alkalinity, for a great part if not the greatest part of the alkaline reaction is due to the cellular constituents of the blood. Drouin (5) has shown that changes in the alkalinity of the circulating blood can be determined by measuring changes in the serum; and Zuntz (*l.c.*), Peiper (*l.c.*), and Winternitz (*l.c.*) have proved that the alkalinity after coagulation remains constant. Wright considers that his own experiments confirm these results. These facts being demonstrated, the principles underlying the use of serum are satisfied.

A brief survey of the extensive literature on hæmalkalimetry will convince one that a completely satisfactory clinical method has not yet been proposed. It is claimed for Wright's method that it has the advantages of simplicity of technique, that it obviates the necessity of diluting the blood, and that it overcomes the manifest physical difficulties associated with titration of a fluid containing red blood corpuscles. Therefore, if the method fulfills its promise of sufficient accuracy for comparative studies, it should be of clinical value.

Although Wright in his original article only gives the results of estimates of the normal alkalinity, he later (6) showed by this method that scurvy was an acid intoxication, and that in this disease the blood alkalinity was represented

[1] I desire here to acknowledge my great indebtedness to Dr. Boggs for his kind assistance in directing this work.

by values of $\frac{N}{90}$ or $\frac{N}{100}$. Luff (7) considered the method satisfactory for measuring the alkalinity of the blood in gout. Moore and Wilson (8) object to the use of litmus paper as an indicator.

We have used the method as described; but have made it a rule to take blood from patients at practically the same hour, 11 a. m. to 12 m., so as to render constant any effects due to digestion, and have uniformly made our readings three to four hours later. Also instead of the series of watch glasses, the water color palette has been employed to hold the acids and for mixing. Excluding all preliminary experiments in acquiring a constant technique, we have made 55 readings on a total of 37 individuals, including normal persons and patients afflicted with various diseases, such as the acute fevers, diabetes mellitus, tuberculosis, infectious arthritis, cirrhosis of the liver, nephritis, leukæmia, pernicious anæmia, and malignant neoplasm. In most of these diseases rather complete studies have been made by various investigators using different methods, and although the exact quantities given differ according to the method employed, there is a fair unanimity in the general results. We therefore have a basis on which to compare our results.

In two cases we got very low values: $\frac{N}{100}$ in a case of pernicious anæmia just before death, $\frac{N}{90}$ in a case of acute lymphatic leukæmia. The latter case had been followed for six days, from the day of admission to the hospital to death. On the day of admission the alkalinity was represented by $\frac{N}{60}$, while on the sixth day, just before the *exitus lethalis*, it was $\frac{N}{90}$. It is interesting, however, and rather important to note that both these cases presented such striking symptoms of acidosis that the diagnosis of "acid intoxication" was made by the visiting physician on inspection of the patients as they lay in the ward. Also the urine in both cases contained acetone bodies. One other case of pernicious anæmia showed an alkalinity varying from $\frac{N}{40}$ to $\frac{N}{50}$, while several cases of striking secondary anæmia gave values never lower than $\frac{N}{40}$. One case of jaundice, with bile-tinged blood serum and marked cachexia, gave by this method values never below normal, although it is generally agreed that both jaundice and cachexia are associated with reduced alkalinity. We had no cases in which the alkalinity was higher than $\frac{N}{30}$. Two cases of diabetes mellitus, without symptoms of acid intoxication and without acetone bodies in the urine, gave normal readings. Two cases of cirrhosis of the liver, studied from day to day, occasionally showed an alkalinity of $\frac{N}{50}$, but on most days it was $\frac{N}{40}$, and as $\frac{N}{40}$ is normal, we do not feel justified, for reasons to be shown later, in drawing conclusions from such an inconstant slight reduction. Most conditions showed alkalinity within the "normal" limits.

Very early in our investigations it was found advisable to eliminate subjective influences as far as possible. To this end, we took on the same day blood from different patients, almost always including one normal, had the capsules listed and renumbered by a colleague, and then estimated the alkalinity of the various sera without knowing to which individual each capsule belonged. The relative insensitiveness of litmus in the presence of carbonates was a constant source of trouble in the exact determination of the saturation point; for example, with a mixture of serum and $\frac{N}{35}$ acid there would be a faint purple tinge to the drop on the litmus, while with $\frac{N}{40}$ acid the drop would be blue. Having determined a fixed point in this gradual change of color from red to blue as our end reaction, we made it a rule to repeat each titration one or more times, and it was here that the shortcomings of the method were most apparent in the non-concordance of the results of repeated titrations of the same specimen at intervals of only a few minutes. Frequently the difference of reaction caused by a change from $\frac{N}{35}$ to $\frac{N}{40}$ or $\frac{N}{45}$ acid was so slight that a great element of imagination was necessarily introduced. If we express the terms $\frac{N}{35}$, $\frac{N}{40}$, and $\frac{N}{45}$ as actual sodium hydrate, this variation amounts to 14 to 22 per cent. The blood alkalinity in disease varies within narrow limits, and it is evident that a method with this amount of inherent error is hardly of sufficient accuracy to be of clinical value. As a matter of fact, in most of the diseases investigated, we have found the readings to fall within the limits of "normal variation" by this method.

When one attempts to explain the inaccuracy of this method, several factors must be considered. Is litmus paper a good indicator? While we shall not attempt in this note to discuss the nature of the chemistry of the blood, it is necessary to state that the blood is not a simple chemical solution, but consists of a solution of complex salts. It contains no free hydroxyl (OH) ions, but its alkaline reaction to litmus is probably due to basic carbonates and phosphates combined with protein molecules or weak acids. It must be remembered that although blood reacts alkaline to litmus, and more so to dimethyl-amido-azo-benzol, it is neutral or acid to phenolphthalein. The physiological activity of the cell protoplasm demands that the circulating nutrient fluid maintain a fairly constant balance, and the variation produced by disease, unless it cause the death of the cell, must always be within narrow limits. Hence, without considering the theoretical basis of indicator reactions, it is at once apparent that any indicator to be of value in hæmalkalimetry must be delicate and must show a definite end reaction. It is a well-known chemical fact that litmus does not show a sharp line of neutrality in the presence

of carbonates. It gives neutrality with carbonates at an intermediate point between the bicarbonate and the normal carbonate, and with phosphates at an intermediate point between the monobasic and the dibasic phosphates. Moreover, the inconstant factor of the viscosity of the blood influences the saturation point of litmus paper; for Hutchison (9) has shown that dilution of serum increases its permeability to litmus paper and thereby causes an apparent increase in its alkalinity as tested by the Haycraft-Williamson (10) method. Therefore, litmus paper is not a suitable indicator for such delicate titrations as are necessary in measuring the alkalinity of the blood. The inherent errors of the Wright method are probably mainly due to the insensitiveness of the indicator.

Furthermore, the mechanics of pipette titration, as employed in this method, would not seem to be satisfactory for even comparative chemical purposes. It is supposed that equal amounts of acid and alkali are used in each titration, but when one considers that the acid solution follows an alkaline fluid (serum) of greater and variable viscosity into a pipette of small caliber, it is obvious that identical amounts are not used, and that the error thus caused must be considerably magnified on account of the small amounts of material employed. If, however, as might be urged, this error should prove to be constant, it need not be considered in comparative work. We are at present investigating this point by using the pipette method with other indicators, but as yet our observations are not sufficiently numerous to justify an opinion as to how much of the error in the Wright method is due to the pipette.

To conclude, then, it is seen that in using the indicator and method of measurement proposed by Wright, the variation inherent to the method includes within its bounds the changes seen in those diseases in which the early recognition of acidosis is important. And when the lowered alkalinity falls definitely without the "normal," we have at the same time clinical and urinary changes which make the condition obvious.

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THE TREATMENT OF GONORRHŒAL ARTHRITIS BY VACCINES.

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In undertaking the study of the treatment of infections by means of vaccines, and especially the control of the administration of vaccines by means of the opsonic index, it has seemed advisable, in order to obtain any clinical evidence as to the value of this method of treatment, that we confine our attention as strictly as possible to one form of infection, or at least that we study as many cases of one condition as possible. We therefore began the study of cases of gonorrhœal arthritis, choosing this lesion for several reasons.

In the first place, it seems most likely that phagocytic or opsonic immunity may play a prominent part in the case of those infections due to the group of cocci to which the gonococcus belongs. Second, this is a condition in which treatment, as at present carried out, is not very satisfactory. Third, it is a local metastatic infection of prolonged course, situated in a position in which the blood supply is not very abundant, and in which, therefore, stimulation of the general mechanism of immunity is probably not very active. In the majority of cases it runs a chronic course, and therefore usually lasts a sufficient time for artificial immunizing processes, if of any value, to be effective. Theoretically, therefore, this would seem to be a most suitable condition for treatment by vaccines,

if the opsonic theory and method devised by Wright are correct.

Furthermore, it is a condition occurring with considerable frequency. The fact that during the past five months 20 patients with gonorrhœal arthritis, in whom the diagnosis was quite certain, applied to us for treatment, shows how frequently the lesion occurs, much more frequently undoubtedly than either the laity or most practitioners are aware, as many of these cases are undoubtedly wrongly diagnosed "rheumatism." It is also a condition which we have been studying for some time, and so were fairly familiar with the course under ordinary forms of treatment.

We have tried to enter upon this study with unbiased minds, though we have endeavored to exercise as much enthusiasm as possible, recognizing that upon this the results of any form of treatment are somewhat dependent. While the number of cases has not been very large, we have endeavored to study each one of them as carefully as possible, with the hope that we might obtain results which would be applicable to other analogous infections.

One difficulty in arriving at any conclusion as to the value of this method of treatment from the reports already made is that in most instances isolated cases of one condition have been reported. It is well recognized that we can never judge of the value of treatment from single cases, especially where the writer has apparently undertaken the treatment with great enthusiasm, owing to the attractiveness of the theoretical considerations upon which it is based. From some of the reports we might judge that the cures by means of vaccines have been almost miraculous, and undoubtedly much harm may be done to the general adoption of this form of treatment by these extravagant claims. From our observations, the value of this form of treatment must be estimated just as is that of any other form of treatment, and in the absence of any large statistics upon which final judgment must rest, we can only arrive at an opinion by as complete a study as possible of a single group of cases, the unfavorable as well as the favorable ones. We, therefore, feel justified in reporting in some detail the cases of gonorrhœal arthritis so far studied.

The technique employed in the estimation of the opsonic index in this series of cases was as nearly as possible that described by Wright. A few points of importance in connection with the work with the gonococcus, however, may be mentioned. The strains of gonococcus used in the estimation of the opsonic index were derived from two sources. One strain was isolated from a knee joint in a severe case of gonorrhœal arthitris with effusion (Case No. III), and the other from a case of gonorrhœal periostitis. Comparisons made between these two strains did not reveal any appreciable differences, and the indices obtained with each of them in the same case did not show any marked variation. But it may be advisable in spite of this fact, to use the organism isolated from the case under treatment. However, there are several difficulties here presented. In the first place, it is often a long and difficult task to isolate the gonococcus from a certain lesion. In the subacute and chronic cases this is especially true. Not infrequently it is quite impossible to find the organism, even in the genital lesions, and much more so in the joints of cases which are definitely gonococcal.

Blood agar was found to be the most satisfactory for the isolation and continued cultivation of the gonococcus. This was prepared by the usual method of mixing human blood with melted agar. About 0.5 cc. of fresh blood was mixed with 10 cc. of agar, and then the tubes were slanted in the usual way. The organism grew very readily on this medium and an abundant growth was obtained in 24 hours. Hydrocele agar was at first employed, but this was found unsatisfactory for several reasons. The growth on this medium is very scanty in 24 hours, and there is always a liability that the organism may die out unless transferred to a new tube daily. On the blood agar, however, the organism remains viable for several days. After repeated transfers are made during a period of several months, the gonococcus will then grow quite as readily on hydrocele agar as on the blood agar. The following points seem to be of interest in regard to the emulsion of gonococci to be used in carrying out the opsonin test.

The age of the culture is of extreme importance. At the most, it should not be over 24 hours, and preferably between 16 and 20 hours, as it was found that in older cultures numerous involution forms were present. Then the strength of the emulsion should be carefully estimated, which can only be done by experience. The most suitable strength is such that in normal serum an average of 6 to 10 cocci per leucocyte will be taken up. The mixing of the emulsion and the breaking up of clumps should be very thoroughly performed. This was accomplished by the method recommended by Wright. It was furthermore found that in the staining of the preparation more time was required than in making tests with the other pyogenic cocci. Hastings' modification of Romanowski's stain was used entirely. The diluted stain was allowed to remain on the slide for at least ten minutes, and more frequently up to half an hour. Even after this period some of the organisms were occasionally found to be very poorly stained, and others showed only as indistinct shadows. It might be mentioned here that similar results were observed when working with Diplococcus intracellularis of Weichselbaum. In counting the organisms, each individual coccus was taken as a unit and all diplococci were counted as two.

It has been held by some writers that certain strains of the organism are endowed with special powers in the production of opsonic immunity. Our experience has been quite to the contrary. The vaccines used by us were prepared from four different strains of gonococcus. Two of these strains have already been mentioned above. The other two were isolated from cases of acute gonorrhœal urethritis. In comparing the results obtained, no distinct difference could be demonstrated in the clinical results or effects on the opsonic index when the patient was vaccinated with a vaccine made of his or her own organism or when a different vaccine was used.

The vaccines were prepared after the method devised by Wright. The strength of each vaccine was usually 600 mil-

lion to one cubic centimeter. In carrying out the treatment, the opsonic index was first determined, and if below normal, the first dose of vaccine was given. This was usually 300 million gonococci. The following vaccinations increased gradually in amount, until 1000 million at one dose was used. No ill effects were encountered, even when 1200 million gonococci were administered at one dose. A slight local reaction always occurred 12 to 24 hours after the first dose. This consisted of slight pain, tenderness and redness at the site of injection. In only one case (No. 15) was this reaction at all marked. This patient suffered for 48 to 72 hours after the injection with marked pain and induration. This occurred after subsequent injections, as well as after the first one, but the reaction diminished in severity with each subsequent dose. After the last injection no reaction occurred.

General constitutional disturbances following the injections were very rare. In fact, in only one case can this be said to have occurred. In this case (No. 12) there was a sharp rise of temperature with general malaise the evening after the second injection. Recovery from this, however, was complete within 48 hours, and no further general disturbance was noted with the subsequent treatment.

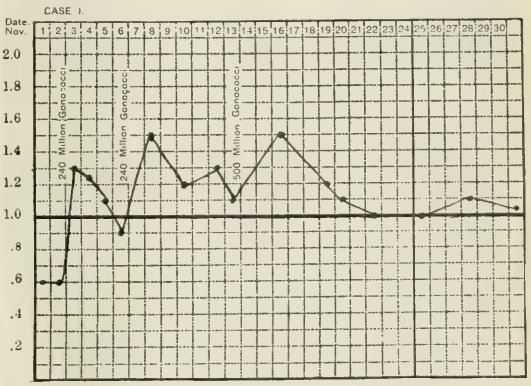
The change in the opsonic index after the treatment varied greatly in individual cases. For example, in comparing Cases 6 and 10, it will be seen they were both vaccinated with the same amounts on January 14, 1907. In Case No. 6 the index gradually ascended and reached the maximum on January 21, when it descended rather sharply. On the other hand, in Case 10, the ascent was sudden, reaching the highest point in two days, and then the index gradually fell. But in both cases the index reached normal in ten days. In studying the charts closely, it will be seen that the rule is a sudden ascent after the reaction, with gradual descent.

The number of vaccinations in the individual cases varied according to the severity and the chronicity. The smallest number was one and the largest eight. The intervals between the injections were controlled by the opsonic index, as stated above, though in most cases the intervals were from seven to ten days. A word might here be said concerning the "negative phase." In none of the cases has this been at all marked. It is possible that the absence of "negative phase" may be due to the fact that daily observations following the vaccinations were not made. But the fact remains that the ill effects of a "negative phase" were not observed clinically and a cumulative "negative phase" was never observed.

The following are reports of 15 cases in which each case has been followed during the entire course. Five other cases have been under observation for short periods, but for some reason it was impossible to follow them longer, mainly because the patients refused to carry out the treatment.

CASE I.—W. J. Dispensary No. 53,765, male, aged 25.

The patient came under observation November 1, 1906. He then complained of pain and tenderness in the right knee. He had had one attack of gonorrhœa several years before, unassociated with arthritis, and a second attack beginning September 3, for which he applied for treatment in the dispensary. On September 10 he began to have pain and swelling of the right knee. This continued and the swelling increased up to the time when seen by us. At no time were any other joints involved. The circumference of the right knee was found to be 8.5 cm. larger than the left. The patella was floating. The knee was held stiffly, there was marked tenderness and the local temperature was elevated. The patient was walking on crutches. He was allowed to continue going about and no other treatment was instituted. The treatment of the urethritis, however, was continued. Following the first injection there was marked improvement in the condition of the knee. Two days after the first injection the circumference of the joint had diminished 2.5 cm. The improvement continued uninterruptedly. By November 10 the pain and tenderness had almost entirely subsided, motion in the joint was good and he walked without a cane. He returned to work on November 19, all signs of joint involvement having disappeared. The urethritis subsided and a slight enlargement of the prostate was the only sign of genital infection remaining. There has been no return of the trouble since.



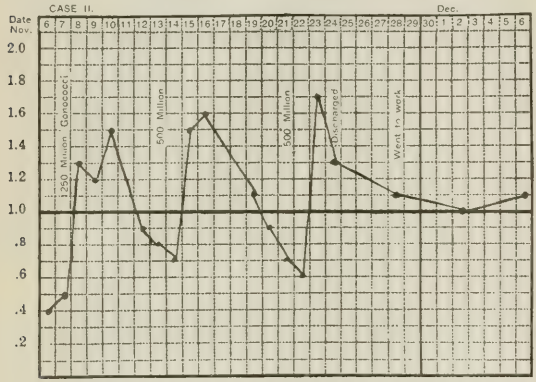
CASE II.—J. O. Surgical No. 19,743, male, aged 40.

The patient came to the hospital for treatment on September 26, 1906, complaining of pain, stiffness, and swelling of the right elbow joint. He had had a fracture of the lower end of the left humerus in December, 1904, from which he never completely recovered. On September 16, 1906, he contracted gonorrhœa for the first time. About one week after the onset of the urethritis he developed some pain and swelling in both wrists. This, however, did not trouble him much and soon subsided, but during the night of September 25, 1906, he began to have severe pain in the right elbow joint. Swelling, pain, and tenderness increased very rapidly and the patient came to the hospital for treatment. On examination the right elbow joint was found to be very much swollen, very tender, the motion limited to a marked degree and the surface temperature elevated. He had an acute urethritis of mild severity.

The joint was treated for several week by local hyperæmia, with only slight improvement. The urethritis was treated by injections and the discharge soon disappeared.

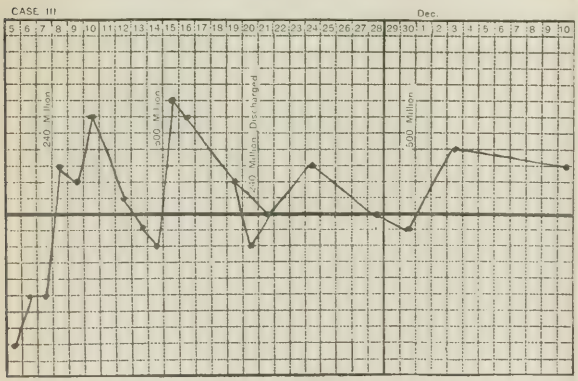
On November 7, 1906, the patient was vaccinated with 250,000,000 dead gonococci. There was immediate improvement. This improvement progressed steadily, with diminution of the swelling and tenderness. Motion in the joint became freer and he was discharged on November 24, and returned to work on November 28. At the time of leaving the hospital, a distinct crepitus could be elicited in the joint, but he did not feel any pain or inconvenience from this, and the patient thought that the motion in the joint was as good as it had been before the infection.

On December 13 the patient returned to the hospital suffering from acute lobar pneumonia. There had been no recurrence of the joint trouble. His pulmonary condition became very grave and he died on December 19. A few hours before death he



complained of a sharp pain in the right elbow, but nothing was made out on local examination.

At the post-mortem examination the right elbow joint was opened. The articular surfaces were roughened and showed signs of a recent severe inflammation. There was a slight amount of fluid present. Cultures from this exudate gave a pure growth of gonococci. Whether the gonococci remained latent in the joint and with a lowering of resistance again became active, of course could not be determined. This case is of great interest, however, showing the persistence of organisms in the joint, even though all signs and symptoms had disappeared.



Case III.—F. J. Medical No. 20,165, female, aged 26.

The patient had never previously had arthritis. During the spring and summer of 1906 she was troubled with leucorrhœa, pain, and frequency of urination, which a physician treated by injections. On September 10, 1906, she had severe chills and fever, and the following day had pains in all her large joints. She entered the hospital on September 18, 1906, complaining of painful and swollen joints. On examination there was pain, tenderness, and increased heat over the left knee, right wrist, and both ankles. Pelvic examination was negative. Although the right wrist and left ankle improved, the fever continued high and irregular and she became very anæmic. Cultures made from the right knee on October 8 were sterile. The fluid was purulent, and smears showed many polymorphonuclear leucocytes, but no organisms.

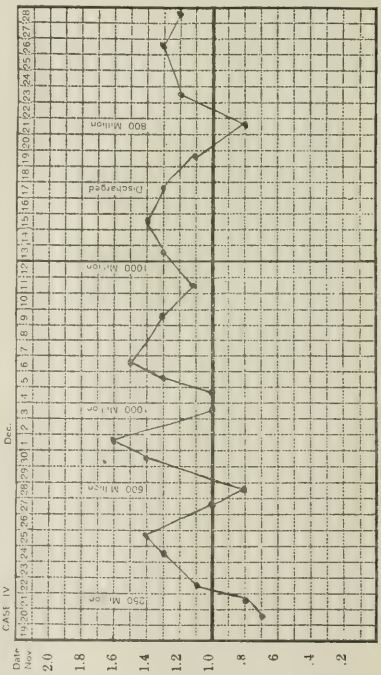
On October 13, cultures were made from the left knee and right ankle and from the blood. On the same date the knee and ankle were opened surgically and thoroughly irrigated. Cultures were again taken from the joints. No growth was obtained from the ankle or blood, but gonococci were grown in pure culture from the knee, both before and at operation.

The incisions healed very well, but the joints remained stiff and painful and the patient's general condition did not greatly improve. The opsonic index was frequently estimated and was found to range between 0.2 and 0.5. On November 7, the first dose of vaccine was administered. The condition improved rapidly and she was discharged on November 20, complaining only of slight stiffness in the left knee. This soon disappeared and all the joints were normal on November 28, 1906. Since then there has been no recurrence.

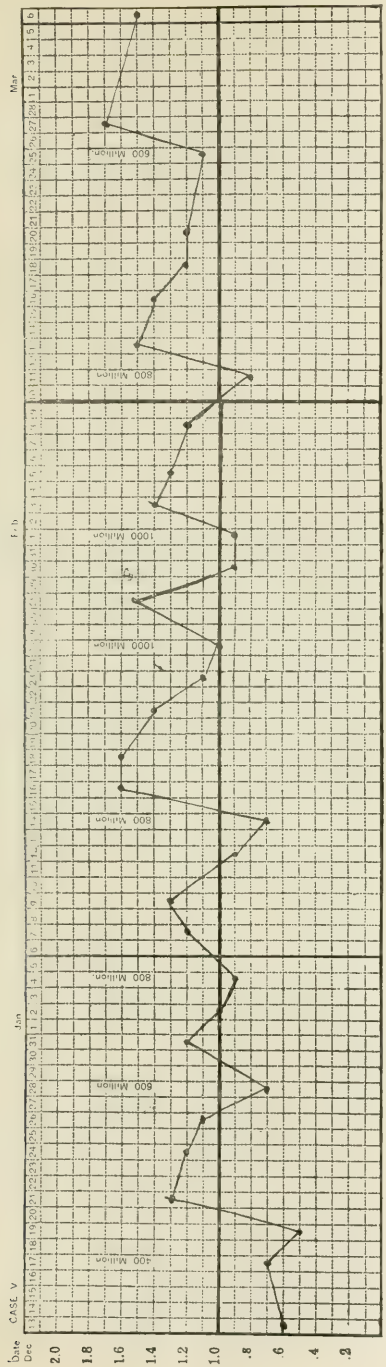
The evidence in this case seems fairly good that the vaccines helped, as improvement was progressing slowly when the vaccines were begun, and afterwards went on very rapidly to complete recovery.

Case IV.—M. S. Gynæcological No. 13,297, female, aged 20.

On October 13, 1906, the patient was operated upon for gonorrhœal pelvic inflammatory disease. Hysterectomy, double salpingo-oophorectomy and appendectomy were performed. The



patient made an uninterrupted recovery from the operation. On November 8 she began to have pain in the left elbow. This was followed by great tenderness, swelling, increased local temperature and fixation of the joint. The joint was treated with rest and local application of ice. But there was no improvement up to November 20, when the pain became so severe as to keep her



from sleeping, and she would not allow the joint to be touched. The opsonic index was 0.7. On November 21, all other treatment was discontinued and 250,000,000 dead gonococci were administered subcutaneously. During the following week the joint improved very much. The patient was out of bed on December 3 and was walking on December 5. During this time, however, she would not allow the joint to be moved and held it in a semi-flexed position. As a consequence, the joint became partially ankylosed, although all other signs and symptoms had disappeared by December 7. The patient was discharged on December 17, and failed to return for further treatment. In January she entered another hospital and was given ether and the joint forcibly manipulated. After this operation, the joint could be freely moved, although slight crepitus was evident. At the present time the patient has full use of her joint and there is no limitation of movement.

CASE V.—D. G. Dispensary No. 81,474, C. male, aged 26.

This patient had gonorrhœa in 1903 and again in August, 1905. Shortly following this last attack he developed arthritis in the knees and joints of the hands. He entered the hospital and was treated with hot air, with slight temporary improvement. He continued to have fresh attacks of arthritis and acute exacerbations of the urethritis. During December, 1905, and January, 1906, he developed prostatitis, double epididymo-orchitis, and vesiculitis. These complications, however, by proper treatment were soon relieved, with the exception of the prostatitis. Up to November, 1906, the arthritis was practically continuous, involving the knees, fingers, hands, sterno-clavicular joints, shoulders, hips, and ankles.

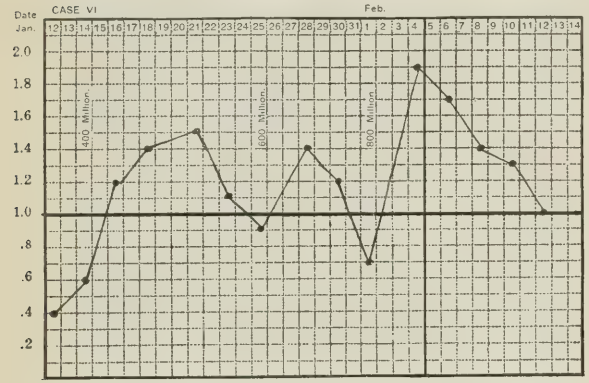
He first came under our observation on December 13, 1906. At this time he walked with a cane. There was pain and tenderness in the shoulders, hips, and sacro-iliac joints, with some diminished mobility. The opsonic index was 0.6.

On December 17, 1906, he was vaccinated with 400,000,000 dead gonococci. The improvement was slow, but quite marked. Within a week he walked without a cane. By January 12, only slight pain in the left shoulder and right hip remained, but he complained of pain on the bottom of the left heel. By January 21 these pains had all disappeared. The genito-urinary condition did not show a corresponding improvement. A chronic urethritis persisted and is still present. The prostate has shown little or no improvement. Since January 21 he has complained of dull pains in the extremities, not well localized in the joints. The patient is very neurotic and it is difficult to tell just how much pain he is having. There is no limitation of motion in any joint. He has complained of pain on the plantar surface of the left heel, but X-rays have shown no thickening or exostosis. It is possible that some slight localized joint or bone involvement still remains, though it cannot be discovered. He still complains of pain, however, and claims that he is unable to go to work. This case is the most resistant one we have had and has offered a good example of the neurotic tendency following gonorrhœal arthritis. The patient has persisted in having intercourse during the treatment and has undoubtedly been reinfected. This case shows the slight value which vaccines may have in the treatment of acute and subacute urethral affections.

CASE VI.—S. W. Surgical No. 20,168, female, aged 46.

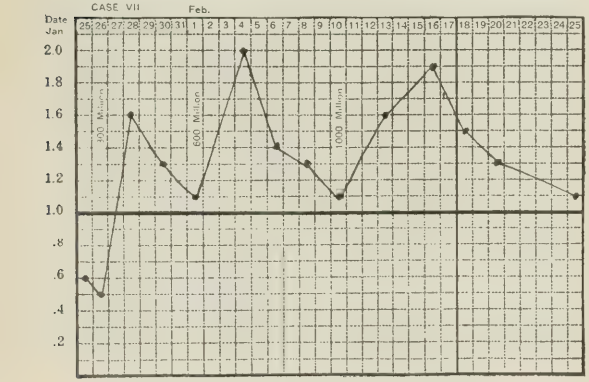
On December 14, 1906, the patient developed pain in the right hip. During the same day this disappeared, but the right shoulder became involved. This joint was very painful, and she could not use it. She came to the hospital on January 7, 1907. There was no history of gonorrhœa or acute articular rheumatism. The right shoulder was enlarged, tender, very painful on movement and there was increased local temperature. Smears taken from the vagina showed typical gonococci. White blood

cells numbered 9040. The opsonic index was 0.5 to gonococcus. On January 14, 400,000,000 dead gonococci were injected subcutaneously. There was immediate improvement and the patient was discharged on January 28, 1907, and returned to work on February 4, with perfect motion restored and no pain. There has been no return of the symptoms since.



Case VII.—H. K. Dispensary No. 11,266, D., male, aged 30.

The patient has had four attacks of gonorrhœa. The last was in October, 1906. Shortly after this he developed pain in the thyroid cartilage, which lasted for some weeks. In November, 1906, he had pain in the lower dorsal vertebræ. There was no local sign besides tenderness and pain on movement. In December the sacro-iliac joints became painful and at the same time the right ankle was very much swollen and tender. He continued in about this condition until first seen by us on January 25, 1907. At this time the right ankle was swollen, red, tender, and the surface temperature was elevated. The joints of the first and sec-



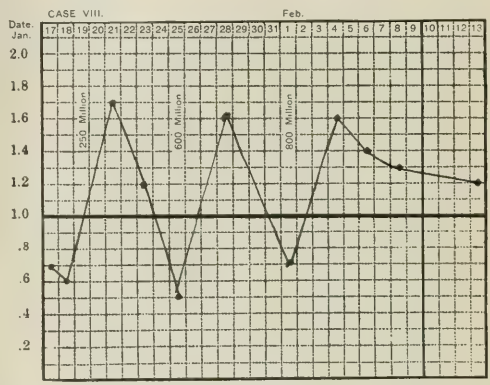
ond toes of the left foot and the little finger of the right hand were in a similar condition, while the sacro-iliac joints were painful and tender. He was compelled to use two canes. His opsonic index was 0.6 to gonococcus. An injection of 300,000,000 dead gonococci was immediately given. The patient began at once to show slight improvement. On February 7, all the joints had cleared up, except the sacro-iliac joints and the right little finger, and he had dispensed with his canes. Very soon the signs in those joints also disappeared, and but a slight capsular thickening of the middle joint of the right little finger remained. All objective signs in the sacro-iliac joints disappeared, but he still has a little pain over the sacrum in the morning on arising. He returned to work on February 16.

The genito-urinary examination when first seen by us revealed a chronic urethritis and prostatitis. This was treated by prostatic massage, during the time of vaccination. This improvement in the prostatic condition was very slow and the vaccination seemed to have very little effect on it.

Case VIII. C. S., male, aged 19.

The patient contracted his first attack of gonorrhœa in November, 1906. This was followed in a few weeks by pain, swelling, tenderness, and redness with increased temperature of the left wrist and the right ankle, while many other joints in the body were attacked very slightly in a fugaceous manner. He was treated in another hospital for some weeks with little or no improvement.

He was first seen by us on January 17, 1907, when the left wrist and the right ankle were much swollen, tender, reddened and there was increased local temperature. His other joints were painful at times, without objective signs. His opsonic index to



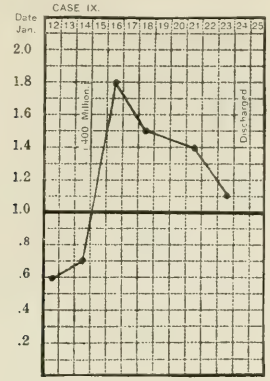
gonococcus was 0.6. On January 19, he received his first vaccination of 250,000,000 dead gonococci. There was a gradual improvement at first. He felt very much better in general health, although the joints did not show much improvement until after the second vaccination on January 25. Then the improvement became very marked and he returned to work on February 8, 1907. There has been no recurrence since.

Case IX.—C. A., Medical No. 20,608, male, aged 36.

The patient had gonorrhœa four times, the last attack in March, 1906. He never had rheumatism before. On December 29 he began to have pain in the lumbo-sacral region of the back, and in the right hip. This was followed by swelling, pain, and stiffness in both ankles and knees, which confined him to a chair until January 7, 1907, when he entered the hospital.

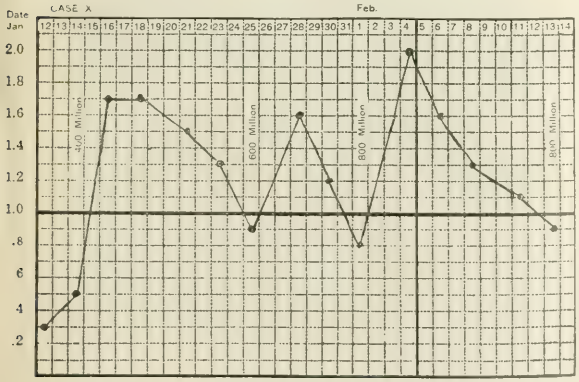
On examination the right knee and ankle were very much swollen, tender, and red and there was increased surface temperature. Genito-urinary examinations showed chronic urethritis and prostatitis. The opsonic index was 0.6 to gonococcus. A subcutaneous injection of 400,000,000 dead gonococci was given. There was some improvement and the patient was discharged on January 24, 1907. The improvement continued and there has been

no return of the arthritis. On the other hand, the genito-urinary condition has shown little or no improvement.



CASE X.—O. K., male, aged 26.

In November, 1906, the patient contracted his first attack of acute gonorrhœa. This was followed in a few days by pains in all his joints. At first there was no special localization, but it soon settled in the right knee joint. This became very much swollen, painful, exquisitely tender, and movement was much limited. He had a temperature of 103 degrees Fahrenheit, and there was a local elevation of temperature over the joint. His condition became progressively worse. The temperature ranged between 100° and 103° F. The joint continued to enlarge and there was fluctuation present. This was practically the condition of the patient when first seen by us on January 12, when the opsonic index to gonococci was 0.4. He was given his first vaccination on January 14, 1907. This was followed by immediate, although slight, improvement. The temperature became normal and remained so after 48 hours. The tenderness and pain subsided and the patient was out of bed on January 25 and was walking about with a cane on January 29. There remained some swelling and stiffness of the joint, which gradually disappeared and the joint regained its former condition, except for some thickening of the capsule. The urethritis had practically disappeared before vaccination was commenced.

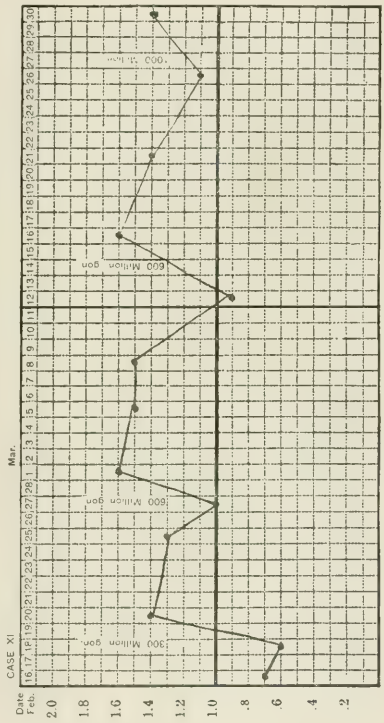


CASE XI.—N. B. Hospital No. 57,936, male, aged 35.

The patient has had gonorrhœa six times. The last occasion was in November, 1906. About December 1 he began to have pain in his hip and this soon involved his other joints in a mild degree. The right ankle grew worse and he entered the hospital on February 1, 1907.

On examination the patient was found to have swelling, tenderness, and slightly increased temperature about the right ankle. There was some morning urethral discharge, chronic urethritis, and prostatitis.

Treatment by Bier's hyperæmia method was begun, but the patient showed no improvement. At the same time urethral irrigations and prostatic massage were instituted. On February 16, 1907, the opsonic index was found to be 0.7 and on the 18th 0.6. At this time the former treatment was discontinued and vaccination begun, with a first injection of 300,000,000 dead gonococci. The improvement, although slow, was continuous. The ankle joint soon became normal, but the prostatitis was more resistant and patient was discharged on March 30, 1907.

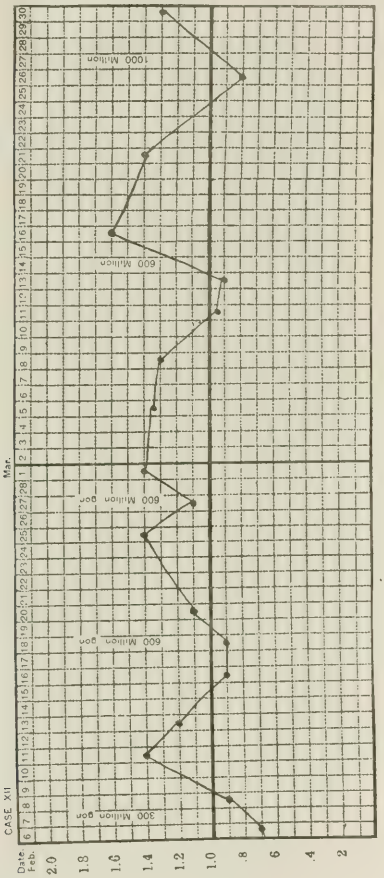


CASE XII.—C. B. Hospital No. 57,952, male, aged 35.

The patient contracted gonorrhœa on November 16, 1906. This gave him very little immediate trouble, but about January 15, 1907, he began to have pain in the lumbo-sacral region and both hips. The knees and ankles became swollen and tender and the patient entered the hospital on February 3. On admission there was a great deal of pain and tenderness over the sacro-iliac joints and in both hips, especially the right. The left knee was swollen and tender, and the patella was floating. The left ankle was much swollen, hot, tender, and red. On genito-urinary examination there was found to be chronic urethritis and prostatitis. The opsonic index was 0.7 to gonococcus. The sacro-iliac and hip joints were treated by the application of a plaster jacket, which

the patient promptly took off. The other joints were treated with hot fomentations, and the genital condition by irrigation.

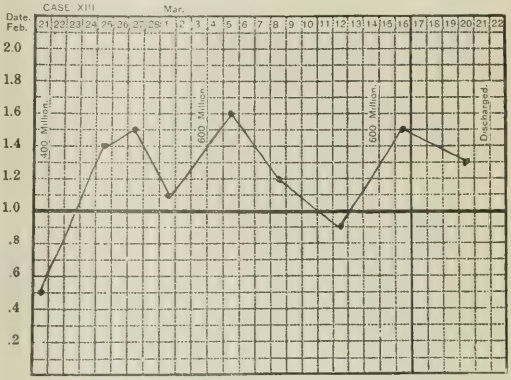
On February 7, 1907, the first vaccination of 300,000,000 dead gonococci was given. There was slight but immediate improvement. By February 21, the ankles and knee had returned to a normal condition. The sacro-iliac and left hip joint showed very slow progress, although the patient was up in the chair on February 22, and even in these joints there was, however, distinct improvement, and the patient was discharged on March 30, as he refused further treatment. The genito-urinary condition had shown steady improvement.



Case XIII.—D. M. Medical No. 20,780, male, aged 32.

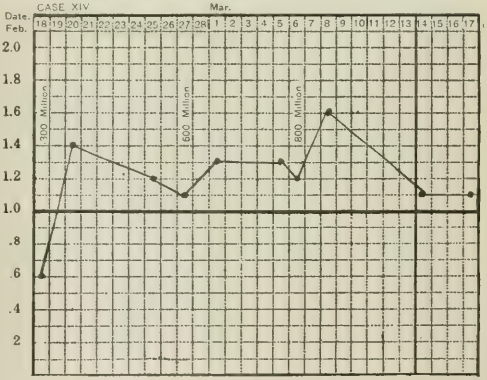
In the early part of December, 1906, the patient contracted his first attack of gonorrhœa. This was followed on December 28, by sudden pain in the left wrist. This became swollen and reddened. Later the middle finger of the right hand was involved and he had transient pains in all his joints. He was not confined to bed, but was compelled to give up his work. There was no improvement, and the patient entered the hospital on February 19, 1907.

On admission the left wrist and hand were very much swollen, reddened, painful, and tender, with increased local temperature. Voluntary movement was absent in the wrist and fingers, while passive movement was very painful. The patient was vaccinated on February 21, with 400,000,000 dead gonococci. There was apparently immediate improvement. Within a few days the redness and pain had disappeared and the swelling and tenderness were much diminished. He was soon able to move his fingers voluntarily to a slight extent. All the signs gradually subsided except the limitation of movement, which persisted to some degree, when the patient was discharged on March 21, 1907. Since then the joint has practically regained its normal condition.



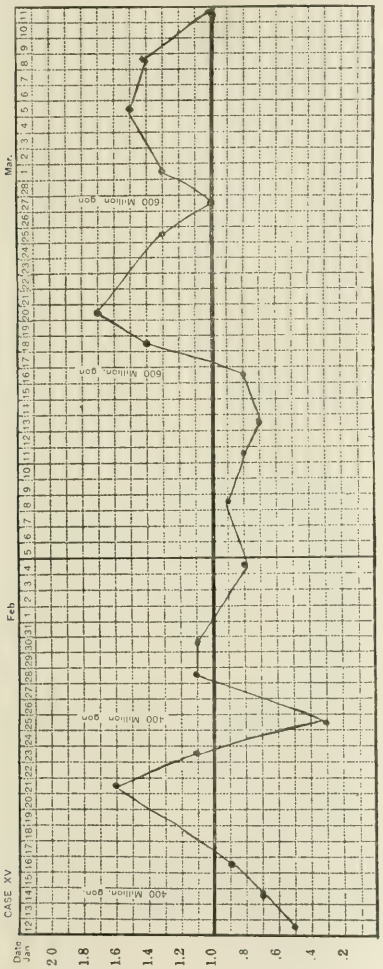
Case XIV.—A. D. Surgical No. 20,209, female, aged 32.

For the past two years the patient has suffered from a persistent leucorrhœa. On January 24, 1907, she began to have pain in the right ankle. This increased very rapidly until the pain was intense. The whole foot became swollen to a marked degree and she had a temperature of 103° F. The patient was admitted to the hospital on February 12. On examination the right foot and ankle, which were the only joints involved, were very much swollen, very painful and exquisitely tender. There was redness and increased local temperature. The motion was



very limited and the patient was unable to walk. Gonococci were not demonstrable in the vaginal discharge. On February 18, 1907, the opsonic index was 0.65 to gonococcus and she was then vaccinated. The improvement was immediate. The local signs of inflammation soon subsided and patient was walking on March 5, and was discharged on March 8. At this

time there were no local signs, but on walking there was some pain in the right instep. Before the onset of the arthritis there had been very marked flat feet. A support was given the patient for the right foot, which gave great relief, and there has been no recurrence of the inflammatory condition.



CASE XV.—J. P. Male, aged 41.

When the patient was 20 years of age he had an attack of gonorrhœa, which lasted ten days and was uncomplicated. He did not have any return of the symptoms until June 1, 1906. At this time he developed an acute urethritis, the discharge from which contained gonococci. In July, he suddenly began to have pain in the left knee joint. This became very much swollen and tender and there was a good deal of redness. During the summer the pain and redness subsided, but the swelling remained. In September a plaster cast was put on, keeping the knee in an extended position. This was removed in October, as the leg had become very much swollen and there was a good deal of pain present. The œdema of the leg disappeared, leaving the knee still swollen and painful. It remained in this condition until seen by us on January 12, 1907.

Examination at this time showed the left knee joint to be very much swollen, circumference 44 cm., that of right knee joint 35 cm. There was tenderness and marked limitation of movement. Genito-urinary examination showed a chronic urethritis, with a morning discharge, and a chronic prostatitis. The opsonic index to gonococcus was 0.55. On January 14 he was given 400,000,000 dead gonococci subcutaneously. The pain in the joint disappeared within a few days. The urethral discharge, however, became more profuse at first, but after seven days it ceased altogether. The swelling slowly subsided and the motion improved, but the treatment was discontinued from January 29 until February 15, as the patient was suffering from influenza.

On February 16 the circumference of the left knee was 38½ cm. and the motion was slowly improving. By February 27 there were no signs of inflammation and massage was advised. This, however, caused a good deal of pain over the anterior border of the tibia and had to be discontinued. By March 5, the right knee joint had diminished to 37 cm. and the movement was gradually improving. Since that time this has steadily increased and there has been no return of the acute symptoms. At present the knee can be bent almost to a right angle and the patient is going about very much pleased with the result. The prostatitis, however, has shown very little improvement since the treatment was commenced, although prostatic massage has been carried on concurrently.

This is the only case where local reaction to any extent was encountered at the point of vaccination. After the first two vaccinations there was marked tenderness, redness and induration about the site of injection. This, however, did not extend further, and after the last two vaccinations the effect was nil.

CHART OF CASES.

No.	Name.	Age.	Sex.	Duration of illness before vaccination.	No. of vaccinations.	Average interval.	No. of days under treatment.	No. of days before returning to work.	Range of opsonic index.
						Days	*Days*	*Days*	
1	W. J.	25	Male	8 weeks	3	6	18	18	0.05 to 1.45
2	J. O.	40	"	7 "	3	7	17	21	0.6 " 1.55
3	F. J.	26	Female	8 "	4	8	23	23	0.2 " 1.6
4	M. S.	20	"	2 "	5	8	36	..	0.7 " 1.6
5	D. G.	26	Male	18 mos.	8	9	70	30	0.5 " 1.7
6	S. W.	46	Female	31 days	3	9	21	21	0.5 " 1.9
7	H. R.	30	Male	11 weeks	4	10	29	29	0.6 " 1.95
8	G. S.	19	"	8 "	3	9	12	20	0.5 " 1.65
9	C. A.	36	"	17 days	1	..	9	9	0.6 " 1.8
10	O. K.	28	"	7 weeks	4	10	30	..	0.4 " 2.0
11	N. B.	35	"	9 "	4	12	37	37	0.6 " 1.6
12	C. B.	35	"	4 "	5	12	48	..	0.7 " 1.6
13	D. M.	41	"	8 "	3	11	27	27	0.5 " 1.6
14	A. D.	32	Female	4 "	3	8	18	21	0.6 " 1.6
15	J. P.	41	Male	7 mos.	4	15	44	30	0.3 " 1.7

Many interesting points have come up in the study of these cases into which we cannot enter here. As to the question of diagnosis, we may say that in practically all cases this has been quite definite from the clinical course, the association of a genital infection or the isolation of the gonococcus. In Case XIV the proof of the gonococcal nature is perhaps not very convincing, but the clinical course rendered it quite probable.

Having followed these cases from day to day, it is difficult not to feel that the treatment has been of value. We recognize, however, how difficult such conclusions are, and we pre-

fer therefore to publish the cases as they are and allow others to decide whether they will carry out this form of treatment or not.

We realize that many cases of gonorrhœal arthritis recover completely under other forms of treatment, but it must be remembered that persisting ankylosis is not at all infrequent. The results in those cases which had been treated by other methods were quite marked. In Case III, although operation had been performed, the progress was very slow until vaccination was commenced. The results in the chronic cases were more marked than those in the acute ones. Case XV was of especial interest on account of the long duration preceding treatment, and the very favorable result that was obtained.

On the whole, our impression is that the vaccine treatment as carried out, has been of distinct value, though we realize that it would require many more cases to make this conclusive. They have been sufficient, however, to justify us in continuing. Those who expect brilliant results or immediate cures following one or two doses of vaccine will be disappointed. We have omitted as far as possible all other forms of treatment, as we have wished to test the vaccine alone. There is no reason, however, why they should not be combined with whatever form of treatment may be considered advisable.

As to the value of the opsonic index in diagnosis and as a guide to the administration of vaccines, we are more undecided. The estimation has been carried out with as careful technique as possible—counting, however, only 50 cells. During the progress of the study, however, work carried on in this laboratory by Dr. Moss, and in which the writers have shared, seems to show that very considerable fallacies exist in our present method of estimating the opsonic content of the blood, and while we are not yet able to say exactly what these limits of error are, they seem to be sufficient to render of little value even considerable variation in the index. It will be seen, however, from a reference to the charts that they resemble quite closely those made by Wright and other observers. In most cases the index has risen following the injection, though at varying intervals. But it must be borne in mind that as the injections were usually made when the index was low, in an irregular chart due to accidental causes, the chances would be greater for the curve to go upward. It is of considerable interest that the first index in practically all of our cases was below 0.7 and in a number of cases 0.5, in one being only 0.2. It is quite probable that such low indices are not due to variations in technique, but are due to real diminution in the opsonic content of the blood. We do not feel, however, that even this can be absolutely decided at present. A very low index may speak for a gonococcus infection.

A reference to our charts will show that the vaccines were usually given at intervals of from 7 to 10 days. Considering the present almost certain inaccuracy in opsonic technique, and the absence of sufficient evidence as to the rôle of opsonins in immunity, it hardly seems advisable that the control of the administration of vaccines by the estimation of the opsonic index should be persisted in. We do not feel that the danger of cumulative negative phases is a real one. In no case have we seen the administration of gonococcus vaccine do harm, and we feel that these cases offer sufficient justification for the treatment of gonorrhœal arthritis by means of vaccines in doses of 500 to 1000 million, administered every 7 to 10 days. Statistics, however, from a large number of cases treated in this way will furnish evidence for or against its value.

THE TUBERCULO-OPSONIC INDEX AND TREATMENT BY TUBERCULIN.

By P. C. Jeans and A. W. Sellards.

(From the Biological Division of the Clinical Laboratory.)

As all who have worked with the tuberculo-opsonic index have found the greatest difficulty in the preparation of a proper emulsion, we have spent considerable time preparing emulsions according to the various methods advised by various observers, in the attempt to procure a perfectly homogeneous suspension. The sources of the tubercle bacilli with which we have worked were: (a) crumbs obtained from Dr. Baldwin, of the Saranac Laboratory, which were secured by filtering a broth culture of the tubercle bacillus, and (b) a glycerine agar-agar culture obtained from Dr. Ford, of the Bacteriological Laboratory of the Johns Hopkins Hospital, and said to be directly descended on artificial cultivation, from an original culture obtained from Koch many years ago.

In the preparation of the emulsion according to the directions of Wright and Douglass,[1] the bacteria should first be heated to 100° C. to destroy their power of clumping, and then ground in an agate mortar with 0.1 per cent salt solution, any stronger solution inducing spontaneous clumping. The remaining clumps are then removed by centrifugalization. Later Wright advised the use of 1.5 per cent salt solution to avoid spontaneous phagocytosis. As the heating of the bacteria causes extreme clumping, the grinding becomes a tedious and time-consuming process, but gives a homogenous emulsion containing a few clumps, many isolated bacteria, some dust particles and many fragmented cells. Considerable difficulty is encountered in enumerating these fractions of cells in phagocytic preparations. We find that some observers have counted each fragment as one bacillus; others have attempted to estimate the fractional parts of bacilli. Either method offers considerable chance for error. In our experience we found that we could handle smaller quantities of bacilli and with

[1] Proc. Roy. Soc., Lond., 1904, LXXIV, 161.

less danger of contamination when we substituted for any of the shaking devices or the agate mortar a test-tube 5 cm. long and 5 mm. in diameter, made from heavy glass tubing. We made a pestle from a glass rod 3 mm. in diameter. The avoidance of contamination becomes of paramount importance, since, after the emulsion is once obtained, it will be clumped again if heated for sterilization.

The only method by which we have been able to separate the bacilli without causing fragmentation is to emulsify the living bacilli, thus avoiding the extreme clumping caused by heat. The emulsion is prepared in the same way as for a living staphylococcus emulsion by rubbing up the bacilli in a little salt solution with a heavy platinum wire or small glass rod. In order to dispense with the precautions necessary in working with a living emulsion we sought a means of sterilizing the emulsion without causing clumping. According to Kolle and Wassermann[2] tubercle bacilli are killed in a few hours by direct sunlight. We have found that an emulsion in salt solution when exposed to the direct sunlight is killed in at least ten hours. The emulsion, prepared in this manner, has the following advantages:

1. The separation of the bacteria is effected without fragmentation and with scarcely more work than is required for a staphylococcus preparation.

2. Sterilization is effected without clumping.

3. When the concentration is sufficient to give a count of 5-8 bacteria per leucocyte, the cloudiness is scarcely discernible to the naked eye, in contrast to the milky emulsions usually employed.

After our emulsions were once obtained by either of the above methods, spontaneous clumping has not been a troublesome factor in either 0.1 or 1.5 per cent salt solution. We were not able to determine that the concentration of the salt solution between 0.1 and 1.5 per cent has any influence on spontaneous phagocytosis,[3] at least with the cultures employed by us.

We have always prepared a leucocytic emulsion from the leucocytic cream obtained by centrifugalization, attempting to secure uniform distribution of the leucocytes. We have collected our serum samples in the usual way, and have incubated our phagocytic preparations, generally for fifteen minutes, observing the usual precautions. We secured satisfactory graduation marks on our pipettes by a method suggested by Barber. A very delicate, almost capillary, glass hair is dipped into Brunswick black. On the capillary pipettes it makes a sharp, definite line, in contrast with the broad diffuse marks usually obtained with a blue grease pencil. The smears were made as advised by Wright.

We fixed our smears by covering with methyl alcohol for 30 seconds and stained with carbol-fuchsin for one to two hours at 37° C., decolorizing with 95 per cent alcohol three to four minutes, and counterstaining five to ten minutes with saturated aqueous methylene blue. Both hot carbol-fuchsin and the use of acid as decolorizer were avoided on account of the injury and distortion caused in the preparation, especially to the leucocytes.

Limits of Error.—As the variation of the count in individual leucocytes ordinarily varies markedly (even with low indices) the average count in 50 leucocytes is subject to considerable variation. In many preparations the leucocytes collecting along the edge of the smear contain distinctly more bacteria than those toward the center of the smear. Thus, by dividing a slide into three sections by transverse lines we found that the section at the end of the smear contained 282 bacteria, the middle section 107, and the first section 140 bacteria in 50 leucocytes. That the bacteria counted at the end of the smear were not mechanically superimposed was shown by control preparations with salt solution in which the leucocytes were everywhere free from bacteria. Ridges of leucocytes may occur almost anywhere toward the end of the smear, making it impractical to count control preparations a comparable distance from the end of the smear.

The following figures show the variation which may occur in the same slide and in duplicate preparations from the same serum sample. (a and a′ are counts on various parts of two slides made from duplicate preparations of the same tube of serum; b and b′ from duplicates of a serum sample collected from a case of tuberculous peritonitis with fever):

A.

	Bacteria in 50 leucocytes.			Total
a	282	107	143	
a′.....	288	235	204	1259
b	223	147	115	
b′.....	203	251	126	1065

B.

a	118	144	138	
a′.....	96	181	130	807
b	134	199	144	
b′.....	143	149	130	899

These counts were made after an experience of over six months, during which time a number of tuberculo-opsonic indices were estimated almost daily. Some differences are to be expected in the two series of counts, as no two men can employ exactly the same technique, but if the method is of value the relative counts should be the same. The opsonic indices obtained by each of the men, if we consider the total cells counted by each, do not show extreme variation. In one case 0.8 and in the other case 1.1. But when we come to consider the individual 50's of cells counted, the variation and inaccuracy appear. We may get indices in A's preparation from 0.4 to 2.34, or if we only take comparable parts of the slides, 0.56 to 2.34. In B's preparation we get variations on comparable parts of the slide from 0.82 to 1.49, or if any parts of slides be considered 0.71 to 2.07. If we add all the counts together we get $\frac{1964}{2066} = 0.95$.

It is quite evident from these figures that, so far as our counts go, the figures obtained from 50 leucocytes give us no

[2] Kolle and Wassermann: Handbuch der pathogenen Microorganismen. Jena, 1903. Bd. II.

[3] Proc. Roy. Soc., Lond., 1905, LXVII, 215.

idea as to the exact opsonic index. We may suppose that counts of 300 cells are sufficient, as the index obtained from these gives us about 1, or 0.95. But there is no evidence that this is correct. To find the absolute error in the technique it will be necessary by counting many thousands of cells, to find at what limit the error is negligible. Then having this we will have to count different preparations and again find the limits of error as the only errors do not occur in the counting. It is unnecessary to go into this, however. We have said enough to show that the limits of error, in our technique at least—and we have followed the method of Wright as closely as possible—are so great as to render the method inapplicable.

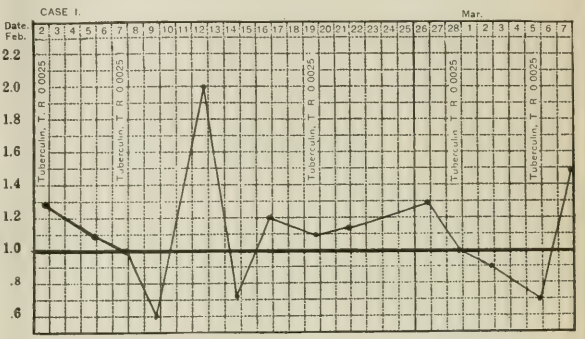
Probably large differences in indices mean differences in opsonic content, but at present we cannot feel that moderate differences mean anything. To count enough cells and to make enough controls of our preparation to render the work accurate places the method outside clinical application. Moreover the evidence that under normal conditions the opsonic content does not undergo considerable variations is not convincing.

But although we feel that our control by the opsonic index is untrustworthy, nevertheless the results obtained by the administration of TR. tuberculin in small, infrequent doses as Wright advises, have given encouraging results. It is possible that the method of vaccination is a correct one, even though the control of the administration by the opsonic index is inadequate. We, therefore, consider it important to briefly report our cases, together with a few opsonic charts which show that the fluctuation in the curves obtained by us do not differ greatly from those obtained by Wright and others.

Theoretically the most suitable cases for treatment with tuberculin would seem to be those cases of localized tuberculosis in which the presence of secondary infection is unlikely or very improbable. Such localizations are found in the glands, bones, and joints. In tuberculosis of the bladder and lupus the rôle of secondary infection cannot, of course, be excluded, but in the cases we have had under observation it has seemed to be of little importance. In pulmonary tuberculosis, however, secondary infection probably plays a considerable part, and it is therefore hardly fair to employ such cases to study the effect of any specific treatment. We, therefore, have confined our attention to the first mentioned group of cases. We have limited the number of cases, preferring to study the opsonic curves as accurately as possible. The following are abstracts of the cases which we have treated by this method. TR. tuberculin was used exclusively. In all cases the dosage was between 0.001 and 0.0025 mgs. In all cases frequent determinations of the opsonic index have been made and an attempt has been made to regulate the dosage and to interspace the administration upon the results of these determinations as advised by Wright. As a matter of fact, however, the doses have usually been given at intervals of from eight to ten days. The occurrence of negative phases has not been marked in any of our cases, and this phenomenon has played little rôle in the treatment. The five curves which we publish have been chosen from our more recent work, when our emulsion was most satisfactory, and after we had had considerable practice in the technique. It will be seen that the apparent regularity is only superficial, and that the variations can partly be accounted for by the laws of chance. Moreover the curve in the case of No. II, in which the result was very unsatisfactory, does not differ materially from that of the case No. I in which the results have been excellent.

Case I.—*Tuberculous glands of neck; pulmonary involvement.*

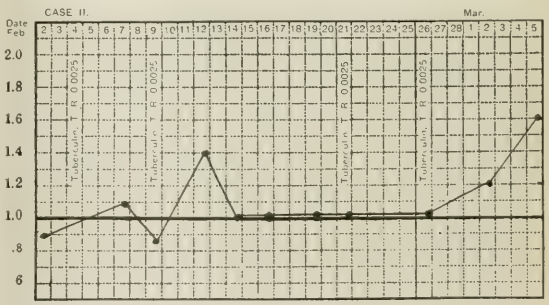
This patient, a young woman, had had a previous operation for enlarged glands on the right side of the neck, but with recurrence. When she came under our observation there were a few large



glands on the left side of her neck and a large group at the apex of the anterior triangle on the right side.

Physical examination of the chest showed signs of a slight tuberculous involvement of the right apex. After four months' treatment, during which time sixteen injections had been given, the glands were still enlarged, but reduced in size and decidedly less firm, and their size on measurement was just one-half what it was when the treatment was commenced. The râles in the chest had disappeared and the patient's general condition was excellent.

During these five months the patient remained out of doors almost constantly, sleeping out at night; she received good food and kept fairly quiet. A portion of the opsonic chart is shown.



Case II.—*Tuberculous glands of neck.*

This patient had had tuberculous glands of the neck removed eight months previously, but the enlargement re-appeared. When she came under our observation the glands on the right side were markedly enlarged. There was no pulmonary involvement. During a period of two and a half months she received nine

injections of tuberculin. There was no decrease in the size of the glands to be made out. The patient thought they were slightly softer, though this was not definite. The patient, rather against our advice, decided to discontinue the tuberculin treatment, and to have the glands again removed by the surgeon. During the period of treatment the patient was employed by day in a telephone office. She refused to sleep out of doors at night, and the food could not be carefully regulated. A portion of the opsonic chart in this case is appended.

CASE III.—*Tuberculous arthritis of right hip and abscess of soft parts.*

The abscess was opened and drained, no attempt being made to reach the joint. The patient was subjected to the usual hygienic measures, good food and fresh air. Two months after the operation and while the wound was healing, the tuberculin treatment was begun. She received six injections in all, covering a period of one and one-half months, when she was discharged from the hospital, the abscess having entirely healed. During the stay in the hospital the power of flexion increased from 15° to 110°; possible rotation in and out increased from 10° each to normal; abduction increased from 5° to 45°.

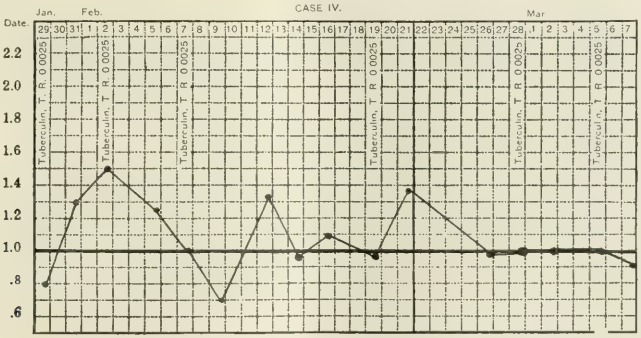
CASE IV.—*Tuberculosis of head of humerus.*

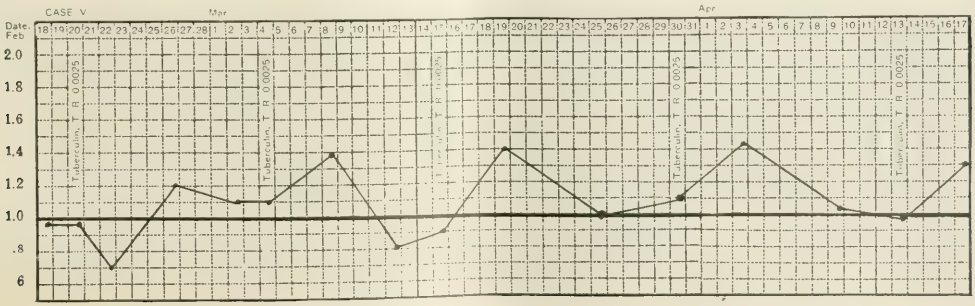
This patient, a boy eight years old, had had his shoulder injured thirteen months previously while at play, but the pain subsided in a week. Following this he had frequent attacks of pain in the shoulder with limitation of motion, these symptoms becoming more marked during the three weeks before coming under our observation. At this time there was found to be atrophy of the arm muscles and limitation of motion, especially in abduction, and weakness. X-ray examination showed a slight erosion of the head of the humerus. He reacted to tuberculin. An exploratory operation showed the focus to be encapsulated, and the case being considered a very favorable one for tuberculin treatment, no incision into the focus was made and the wound was closed.

We have given twenty injections of tuberculin, covering a period of five and a half months. During this time the patient's weight has remained the same. There is still slight atrophy of the pectoral and scapular muscles. The strength of the arm, however, is good and is equal to that of the other arm. There is no pain whatever in the shoulder and there are no tender points. There is practically no restriction of motion, except very slight, on abduction. He plays actively. The X-ray also shows improvement. The arm has not been kept fixed. A portion of his opsonic chart is added.

CASE V.—*Tuberculosis of hip.*

This patient, a young woman aged twenty-nine, had hip-joint disease (right hip) since thirteen years of age. She was well treated and got on fairly well, though with deformity, until 1900, when there was an exacerbation of the trouble and an exploratory operation was performed, but the joint was not opened. Within a few months the pain disappeared. One year later she suffered from tuberculosis of the right wrist, involving mainly the tendon sheaths. This was operated upon and the patient made a good recovery, with quite good functional result. The wrist has given no trouble since. Six months before coming under our observation she began to lose weight, have general malaise and to suffer from pain in the right hip and knee. For two months before we saw her the leg had been held in forced extension, and the pain had become much less. She has now been under treatment with tuberculin for three months, during which time she has had eight injections. During the past month she had had no pain whatsoever, and X-ray examination shows no evidence of any advance in the process, though the deformity due to the old trouble is so marked as to make any decision as to the extent of the present trouble difficult.





Case VI.—*Tuberculous arthritis, ankle.*

The patient had had aching pain and swelling of the left foot and ankle for one month. On examination the ankle was found to be swollen and hot. There was marked tenderness on passive motion, and motion was considerably limited. The X-rays showed quite typical changes as commonly seen in tuberculous joints and the tuberculin reaction was positive, giving a local reaction. During a period of one and a half months he received 5 injections of the small doses of tuberculin, and during this period the swelling pain, and tenderness much improved. The patient, however, was transferred to Bayview Asylum and it was impossible to continue the treatment and observation longer.

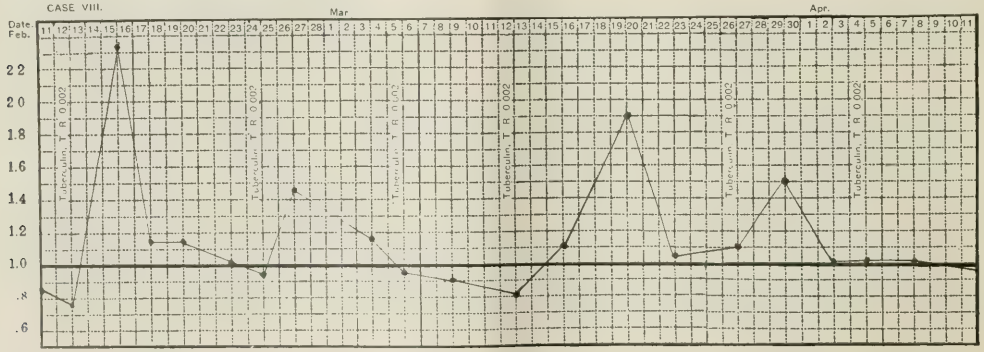
Case VII.—The patient was an old man, aged 80 years, who for three weeks before admission had complained of swelling, pain and tenderness of the left wrist and hand. The onset was very sudden and the early stages were acute. The entire arm below the elbow had become swollen. When first seen, there was very marked tenderness, the wrist was held stiffly and there was marked local œdema. The acuteness of the process suggested some form of acute arthritis, but the X-ray examination showed conditions such as are usually seen in tuberculous joints, and he was given the tuberculin test, which was positive, with a definite local reaction. The treatment with tuberculin was started, giving as in the other cases, small doses of the tuberculin TR. infrequently repeated. Improvement seemed to begin at once. The swelling in the wrist diminished, the tenderness became less and motion in the joint slowly returned. He was kept in the hospital for a month and a half, but the joint was not fixed. At the end of this time he left the hospital, but returned for treatment. This was continued for about three months, and then was discontinued as the patient failed to return for observation and treatment. It is now four and a half months since treatment was commenced. There is still slight limitation of motion in the joint and X-ray examination shows slight erosion of the metacarpal bones, but the condition is markedly improved over what it was when the treatment was commenced. We have advised continuing the treatment and, as he is again having a little pain in the joint, he has consented and the injections have been resumed.

Case VIII.—The patient is a boy aged 12, suffering from lupus vulgaris of about 12 years' standing. At present he has a large patch about 10 x 4 cm. under the chin and a small area about 1½ cm. in diameter on the forehead. This boy had been treated for 5 months and has received 17 injections. The lesion looks markedly cleaner and healthier and the scab formation and suppuration have much diminished. During the past month there has also been some tendency to healing about the edges of the area on the chin, but the patient states that it always becomes better in the spring. The small area on the forehead has not been influenced by the treatment.

Case IX.—This patient was a man aged 39, suffering from tuberculous cystitis of four years' duration. He had had local treatment over a considerable period of time. He was treated for two months and received 8 injections. There was, however, no improvement in the patient's local or general condition. In fact, the local condition became worse. The patient refused to continue the treatment longer. He has since died from a tuberculous meningitis.

The study of these nine cases is sufficient, we think, to justify further continuation of the method of treatment. In none of the cases has the result been miraculous, but in certain of the cases, especially in Cases IV and VII, there seemed to be a very definite relationship between the treatment and the improvement in the patient's condition. That it is important that, in addition to the tuberculin treatment, hygienic measures should be carried out as well, is shown by a comparison of the two cases of tuberculous adenitis. The cases are too few for any general conclusions to be drawn. Other dosage and other interspacing of doses might have been more efficacious, and possibly other forms of tuberculin might give still better results. This can only be decided by the clinical results, and we feel that it cannot be decided by the opsonic curves.

We have employed the opsonic method for diagnosis in a considerable number of cases without obtaining satisfactory results. The diagnostic method described by Wright of heating the serum for the detection of immune opsonins has also not proved of value in five cases in which we have tried it. Lately, with very careful technique and with what seemed to be a very positive result, we obtained an index of 2.4 in a case that was considered to be tuberculous peritonitis, with possibly Addison's disease. Autopsy later showed no tuberculosis present, except an old calcified nodule in one lung.



STUDIES ON OPSONINS.

By William Lorenzo Moss, M. D.

(From the Biological Division of the Clinical Laboratory.)

According to Wright, the immediate object of the vaccine treatment of disease is to so increase the opsonic content of the blood that the bacteria producing the disease may be more readily phagocyted and their noxious influence thereby more speedily ended.

The "index" of this power on the part of the serum for preparing bacteria for phagocytosis, and Wright's method of determining it, have been made familiar to all by numerous publications.

Wright has been contented to raise this index, by his inoculations, to a very slight degree, his early experiments apparently showing that a summation of positive phases (to use his terminology) such as occurs in antitoxic and bactericidal immunity does not occur in the case of opsonic immunity.

The dosage of vaccine which he has employed is purely arbitrary. Why, for instance, should 250 million streptococci be given for the initial dose rather than 2500 million? No experiments, so far as we know, have been made to determine the maximum dose, if we except certain clinical observations of Wright's, few in number, in which too large doses at too frequent intervals caused apparent summation of negative phases.

However this may be, and we feel that possibly a different interpretation may be given to his results, it has seemed important that if the treatment by vaccine is to have any scientific or practical value we must determine (a) if opsonin plays any part in immunity, (b) if we can influence its production in the body, and, if so, by what method we can obtain the most favorable results. In order that these questions may be studied a technique must be devised sufficiently accurate for the purpose and the limitations of which must be definitely known. In the following experiments we assumed that the technique of Wright was sufficiently accurate and employed it with certain additions, to be described later, in studying the above problems.

Furthermore, if the opsonins represent definite immune substances in the ordinary sense, it would seem remarkable that by the introduction of the opsinogen the increase of the antibody in the blood is so very slight. If, for instance, we could increase the opsonin in the blood 100 or 1000, or even 1,000,000 times, as is the case with agglutinin or bactericidal antibodies, this method of treatment might have much more importance.

The following experiments were undertaken to determine to what extent the opsonic content of the blood could be increased. The animals used were rabbits, the organism employed Staphylococcus aureus and control uninoculated rabbits were kept.

The method employed consisted in repeated progressive inoculations: (1) intravenously with dead staphylococci; (2) subcutaneously with living staphylococci; (3) subcutaneously with dead staphylococci.

The results were studied by Wright's method of estimating the opsonin, but it was thought that there might be an increase in the opsonin which would not be detected by this method alone; a sort of supersaturation which might only become apparent when the serum was greatly diluted. It was thought, for instance, that the serum of an inoculated animal in dilution of 1 to 100 might affect a given number of bacteria as much as an equal volume of undiluted serum of an uninoculated animal.

To determine if this might be the case the index was taken with dilutions of 1 in 5, 1 in 10, 1 in 50, and 1 in 100, as well as with the undiluted serum. The technique employed was the usual one, as closely following the method of Wright as possible.

The bacterial emulsion was prepared from a 24-hour agar growth of Staphylococcus aureus, and great care was employed to obtain homogeneous emulsions.

The various dilutions of the serum having been prepared, the preparations were made in the following way: Equal volumes of washed leucocytes, bacterial emulsion and serum (or diluted serum) were mixed in capillary pipettes and incubated at 37° C. for 15 minutes.

Films were then made from these pipettes, stained with Hasting's stain, and the average number of bacteria in each leucocyte was estimated by careful counts of 50 leucocytes on each slide.

The opsonic index was calculated in each case by dividing the number of bacteria contained in 50 leucocytes in a preparation in which rabbit's serum was used by the number of bacteria contained in a like number of leucocytes in a preparation in which a corresponding dilution of normal human serum was employed.

Record was kept of the percentage of polymorphonuclear leucocytes phagocyting in each dilution, as well as of the number of bacteria which they contained, and a curve of phagocytic index was constructed in addition to the curve of opsonic index. This phagocytic index was obtained by dividing the percentage of cells phagocyting in a preparation in which rabbit's serum was employed by the percentage phagocyting in a preparation in which a corresponding dilution of the standard human serum was used.

The records of the observations made during this series of experiments occupy 45 chart sheets and cover over 350 determinations of opsonic index, exclusive of other data collected, so that it is not feasible to include all the records with the publication of this article, but a few illustrative charts will be published and the points given which were brought out by a careful analysis of them all.

Rabbit A was a full-grown, healthy looking female rabbit, under observation from Nov. 7, 1906, to March 5, 1907, during which time it received 10 intravenous inoculations of dead staphylococci. The initial dose consisted of 125 million (approximated by Wright's method), and the dose gradually increased to 4000 millions. Observations of the opsonic index were made of the serum and each of the dilutions of the serum before mentioned, 18 times. At no time did this rabbit appear to suffer any ill effects from the inoculations.

Rabbit B was an average-sized, male rabbit, kept as a control, and at no time received any inoculations. It was under observation from November 6, 1906, to March 13, 1907. The index was taken in all the various dilutions 23 times.

Rabbit C, male, was under observation from December 5, 1906, to February 3, 1907, and received five subcutaneous inoculations of living staphylococci, the index being taken six times. Beyond slight local reaction at the sites of inoculation, this rabbit remained apparently well until it was found dead in its cage one morning. The cause of death could not be determined. Autopsy was negative as far as macroscopic examination was concerned, and cultures were negative.

Rabbit D, male, under observation from December 5, 1906, to March 13, 1907, received eight subcutaneous inoculations of dead staphylococci, beginning with 250 million and increasing to 6000 million. This rabbit showed no ill effects which could with any certainty be ascribed to the inoculations, but looked puny toward the end of the experiments, perhaps a result of the confinement.

Rabbit E, male, under observation from February 5 to March 13, 1907, received two subcutaneous inoculations of living staphylococci, and had the index taken in all the dilutions 13 times.

Chart No. 1 will serve to illustrate how the records were kept. The first two curves under date of November 7, 1906, show the percentage of cells phagocyting in the various dilutions, the solid black representing those in rabbit A's serum, the hollow dots and broken line, those in the preparation in which the standard human serum was used.

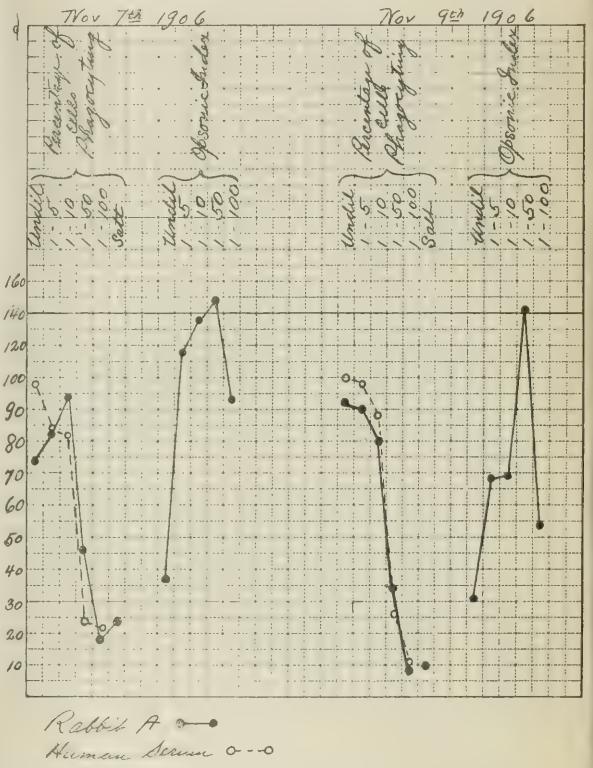
The next curve represents the opsonic index for rabbit A in the various dilutions. Similar observations are recorded under date of November 9.

From the charts, of which No. 1 is an illustration, curves of the opsonic index in all the various dilutions except 1 to 100 were constructed; portions of these curves for rabbits A and B are shown in Chart No. 2.

As previously stated, charts were made showing the curves of phagocytic index as obtained by dividing the percentage of cells phagocyting in the rabbit's serum by the percentage phagocyting in the standard serum. Chart No. 3 illustrates these curves.

From a consideration of all the curves showing percentage of cells phagocyting it is evident that in a general way the largest percentage occurred in the undiluted serum and progressively diminished as the dilution was carried on, as would be expected. There were exceptions to the rule, however, in which the percentage of cells phagocyting was greater

Chart No. 1.



in dilutions of 1 to 5, or even in 1 to 10 than in the undiluted serum. The percentage always fell between 1 to 10 and 1 to 50, though sometimes it happened that the percentage of cells phagocyting and the number of bacteria taken up was greater in the 1 to 100 dilution than in the 1 to 50.

A control preparation was regularly made in which no serum was used, but a corresponding volume of 0.85 per cent NaCl solution, and a record of the percentage of cells phagocyting in it, and the number of bacteria ingested was kept.

In this control preparation the percentage of cells phagocyting and number of bacteria ingested were generally lower than in the 1 to 100 dilution of serum, but the two results ran pretty close together and not infrequently the preparation con-

CHART No. 2.—Curve of Opsonic Index.

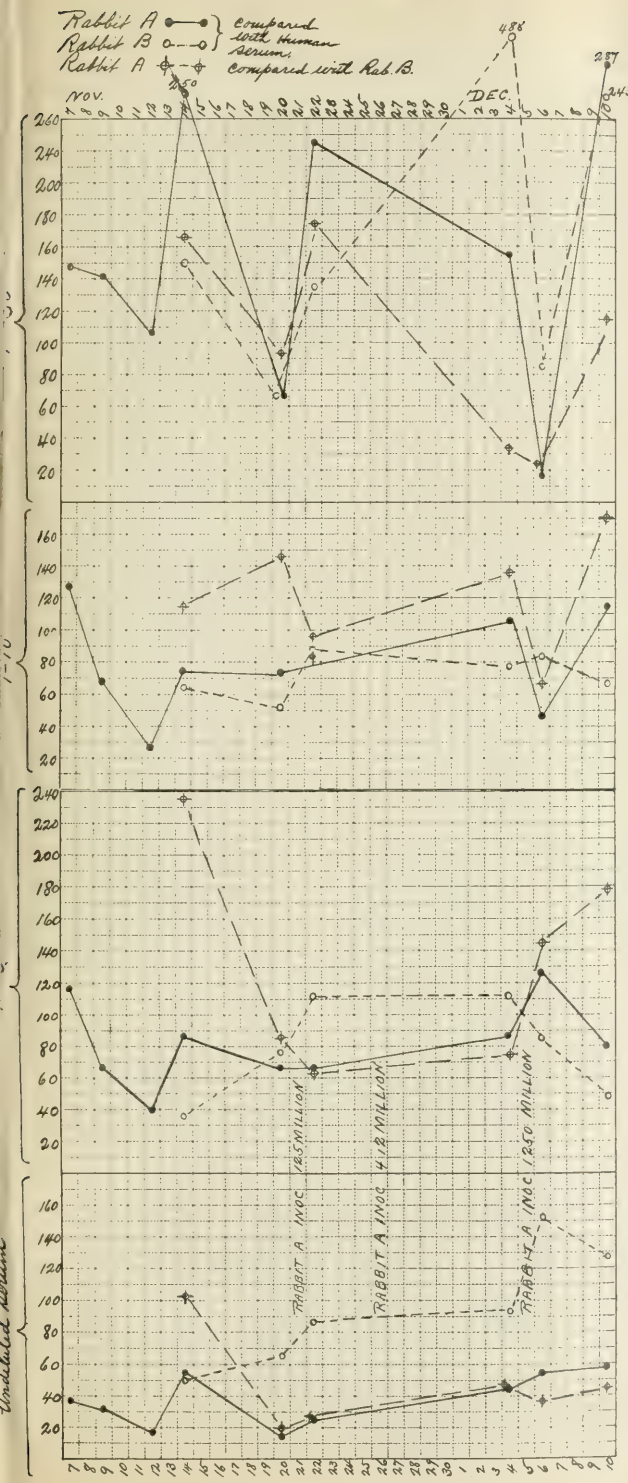
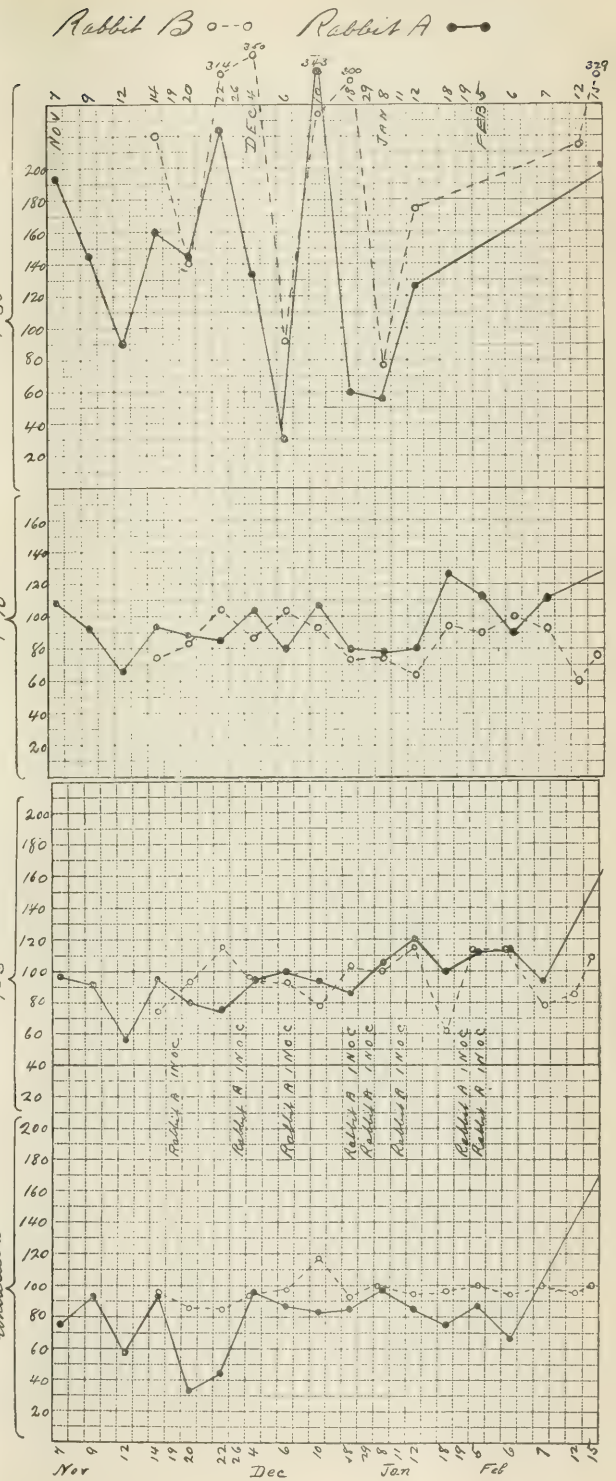


CHART No. 3.—Curves of Phagocytic Index.



taining 1 to 100 dilution of serum, or even 1 to 50 dilution, contained fewer ingested bacteria and fewer active leucocytes than did the control with NaCl solution.

Some of the above statements are illustrated in Chart No. 1, November 7, in which the percentage of cells phagocyting in rabbit A's serum increased from 74 per cent in the undiluted serum to 94 per cent in dilution of 1 to 10, then fell to 18 per cent in dilution of 1 to 100, while 24 per cent phagocyted in NaCl solution. The percentage phagocyting in the standard serum on this date follows the general rule of a progressive decline with dilution.

It may be remarked here that the absolute number of cells phagocyting in any given case seemed to depend largely on the strength of the bacterial emulsion used, and, in the lower dilutions at least, practically all of the cells could be made to phagocyte by using a sufficiently thick emulsion of bacteria, and this observation did not seem at all dependent on overlying of the leucocytes by bacteria, and is, we think, significant. This observation seems to militate against the use of the coefficient of extinction as a means of estimating opsonin.

Only in a general way did the number of bacteria phagocyted run parallel to the number of leucocytes phagocyting. Both diminished with dilution, but no constant mathematical relationship could be made out. As a rule the number of bacteria ingested diminished more rapidly than did the percentage of leucocytes.

In using bacterial emulsions of different strengths, the same percentage of cells may phagocyte, while the number of bacteria taken up may be widely different.

A study of the curves of opsonic index, of which Chart No. 2 is an example, brings out some interesting points. In the first place, four observations were made on rabbit A, November 7, 9, 12, and 14, before any inoculation was given, and it will be seen that if we accept Wright's method of determining the index as accurate, that the index of this rabbit was by no means constant, even before inoculation, the variation in the undiluted serum ranging between 0.18 and 0.56. The same variation in the index of all the other rabbits was noted where a number of observations were made before inoculation.

When we come to compare the curves of opsonic index in the various dilutions, we find, contrary to expectation, that the index as obtained in one dilution is not the same as that obtained in all the other dilutions.

It is difficult to explain this variation. If we take two sera containing different amounts of opsonin, and dilute each to the same degree, whether it be one-half or 100 fold, it seems that the opsonic content would be proportionately diluted, and that the *ratio* which one bears to the other should be the same, no matter in what dilution tested.

In the case of rabbit A the index almost regularly and with striking constancy rises with progressive dilutions, the lowest index usually occurring in the undiluted serum and the highest in dilution of 1 to 50, or 1 to 100. Chart No. 1 illustrates this fact. Reference to the curve of opsonic index on November 7 shows the lowest index 0.37 in the undiluted serum, the highest index 1.49 in dilution of 1 to 50. The curve of opsonic index for November 9 has the same characteristics, the lowest index occurring in the undiluted serum and the highest in dilution of 1 to 50. In other words the serum of this rabbit stood dilution much better than the human serum with which it was compared. This was true, though in a less striking way, of the serum of all the other rabbits. It would require too much space to include all these curves here, but they have been summarized in the following table, No. 1, which shows in what dilutions the maximum and minimum indices occurred.

TABLE No. 1.

Showing in what dilutions maximal and minimal opsonic indices occurred.

Rabbit A.	Min.	Max.
Nov. 7	Undil.	1-50
" 9	"	1-50
" 12	"	1-100
" 14	"	1-50
" 20	"	1-100
" 22	"	1-50
Dec. 4	"	1-50
" 6	1-50	1-5
" 10	Undil.	1-100
" 18	"	1-100
Jan. 8	1-50	1-5
" 12	Undil.	1-5
" 18	"	1-10*
Feb. 5	"	1-10*
" 6	"	1-10*
" 7	1-5	1-10*
" 20	Undil.	1-100
Mch. 4	"	1-100
Rabbit B.		
Nov. 14	1-5	1-50
" 20	1-10	1-100
" 22	Undil.	1-100
Dec. 4	1-10	1-50
" 6	1-10	Undil.
" 10	1-5	1-100
" 18	1-10	1-50
Jan. 8	1-50	1-5
" 12	1-10	1-5
" 18	Undil.	1-5*
Feb. 5	"	1-10*
" 6	"	1-10*
" 7	1-5	1-10*
" 12	1-10	1-50
" 15	Undil. and 1 100	1-50
" 18	1-50	1-10
" 20	1-10	1-100
" 23	1-10	1-50
" 26	1-5	1-100
Mch. 4	1-5	1-50
" 6	1-50	Undil.
" 13	1-100	"

Rabbit C.	Min.	Max.
Dec. 5	1-50	1-100
" 8	1-5	1-50
" 14	1-5	1-100 and undil.
Jan. 10	1-10	1-50
" 14	Undil.	1-50
" 18	"	1-10*
Rabbit D.		
Dec. 5	1-5	1-100
" 8	1-5	1-10
" 14	1-5	Undil.
Jan. 10	1-10	1-50
" 14	Undil.	1-50
" 18	"	1-5*
Feb. 5	"	1-10*
" 6	"	1-5*
" 7	"	1-5*
" 12	"	1-50
" 15	"	1-50
" 18	1-50	1-10
" 20	Undil.	1-100
" 23	1-10	1-50
" 26	Undil.	1-10
Mch. 4	1-5	1-100
" 6	1-50	1-10
" 13	1-10	1-100 and undil.
Rabbit E.		
Feb. 5	Undil.	1-10*
" 6	1-10	1-5*
" 7	1-5	1-10*
" 12	Undil.	1-50
" 15	1-5	1-50
" 18	1-50	Undil.
" 20	Undil.	1-100
" 23	"	1-50
" 26	"	1-10*
Mch. 4	1-10	1-50
" 6	1-50	1-100

* Dilutions higher than 1-10 not made.

As stated in the beginning of this paper, the main object of the experiments was to see to what degree the opsonic index could be raised. An examination of all the curves show that no very high indices were obtained except in dilutions of 1 to 50 and 1 to 100. The results obtained in these dilutions are not considered very trustworthy for reasons to be given

presently. The curves for each rabbit have all been summarized except the 1 to 100 dilution in Table No. 2.

TABLE NO. 2.

Showing maximal and minimal opsonic indices for each rabbit during entire period of observation.

Rabbit A.	Min.	Max.	*Rabbit C.*	Min.	Max.
Undil.	.14	1.49	Undil.	.48	1.31
1-5	.40	3.55	1-5	.26	.94
1-10	.28	3.43	1-10	.64	2.39
1-50	.18	20.14 next 3.20	1-50	.50	3.22
Rabbit B.			*Rabbit D.*		
Undil.	.35	2.34	Undil.	.35	2.81
1-5	.37	2.90	1-5	.32	5.70
1-10	.31	2.75	1-10	.39	2.65
1-50	.02	4.88	1-50	.48	9.39 next 3.45

Rabbit E.	Min.	Max.
Undil.	.48	1.63
1-5	.36	2.80
1-10	.40	1.57
1-50	.40	2.90

Excepting in the dilutions of 1 to 50 and 1 to 100 the highest index obtained for any inoculated rabbit was 5.70 for rabbit D in dilution of 1 to 5. This rabbit received subcutaneous inoculations of dead staphylococci. The next highest index was 3.55 for rabbit A in dilution of 1 to 5. This rabbit was inoculated intravenously with dead staphylococci.

The control uninoculated rabbit B reached an index of 2.90 in dilution of 1 to 5, 2.75 in dilution of 1 to 10, and 2.34 in undiluted serum.

Not only did we fail to produce very high indices, but such high indices as were produced were not maintained for any length of time, and it is difficult to show any relation which they bore to the inoculations.

Furthermore, the index of the control uninoculated rabbit, with the two exceptions mentioned above, showed as great variations as that of the inoculated rabbits. See Table No. 2 showing maximum and minimum indices.

In certain places a suggestive parallelism was noted between the curves of the inoculated rabbits and the control. Instances of this are shown in Chart No. 2 in the curve of opsonic index in 1 to 50 dilution. The index of both the inoculated rabbit and the control went down to a low point on November 20 and December 6, and reached a high point on December 10.

This parallelism suggests very strongly a variation in the opsonic content of the standard serum to which the others were referred rather than a coincident increase or decrease in opsonin in the inoculated and uninoculated rabbits.

Thinking that there might be some difference between the opsonin contained in human blood and in rabbit's blood which would render indices based on a comparison of the two fallacious, the index for rabbit A was calculated, using the serum of rabbit B (uninoculated) as the standard. The curve obtained by this method differed considerably from that which resulted from a comparison with human serum, but the maximum and minimum indices fell within about the same limits, and it could not be seen that inoculation had any more definite influence on this curve than on the previous one. This curve is shown on Chart No. 2 and may be compared with that obtained with human serum as a standard.

Curves were constructed for the other rabbits based on a comparison of their sera with that of the uninoculated rabbit, but the results were not different from those in the case of rabbit A.

The results in the dilutions of 1 to 50 and 1 to 100 were considered untrustworthy, as stated above, because the index in these dilutions represent the ratio between such small numbers of bacteria; for instance, the high index obtained for rabbit A found on November 14 in dilution of 1 to 50 was obtained by dividing 25 by 10; twenty-five being the number of bacteria taken up by 50 cells in the preparation in which rabbit's serum was used, and 10 being the number taken up by 50 cells in the preparation in which human serum was used. The high index obtained for rabbit D on January 10 was the quotient of 37 divided by 15. Here it will be seen that a slight difference in either one of these numbers would make a considerable difference in the index.

As stated, curves of phagocytic index were constructed, but these seemed less reliable than those of opsonic index as a means of estimating the amount of opsonin in the blood, and space will not be taken to include all of them here.

The results of the foregoing experiments seem to cast considerable doubt on the accuracy of the methods generally employed in the estimation of the opsonic index. Wright's method seems inadequate, as do also the methods of using diluted serum, percentage of cells phagocyting, and phagocytic index as described above.

One conclusion seems justifiable, however, from these experiments, notwithstanding the inaccuracies of our methods of investigation; that is, that no very high grade of opsonic immunity can be produced by means of ordinary inoculation procedures, with staphylococci, at least, in a degree comparable to that obtained in antitoxic and bactericidal immunity.

At the conclusion of the above experiments a new series was undertaken with reference to the investigation of certain points. The culture of Staphylococcus aureus used in the previous experiments was an attenuated laboratory culture. It was decided in the new experiments to use a virulent culture and in order to obtain this, the organism previously used was passed in succession through about 10 mice. It was also decided to try a wider range in the dosage, and to control the standard serum used by making simultaneous observations under exactly the same conditions on two other normal sera. This method of control was thought to have an advantage over that of using pooled serum in that it would give information regarding variations in the different normal sera used, and, at the same time, all the advantages of pooled sera could be obtained by using the average of the three normal sera.

Four fresh rabbits were secured for these experiments, and each day for four successive days observations were made on the indices of each before any inoculation was given. Three of these rabbits, G, H, and I, had their indices taken to the same culture of Staphylococcus aureus that was used in the

previous experiments, while the fourth rabbit, J, was tested with the culture which had been passed through the mice.

The indices were first taken with reference to only one of the three normal sera, and later corrected to the average of the three. That is to say, the index was in the first place obtained by dividing the number of staphylococci contained in 50 cells in a preparation in which rabbit's serum was used by the number of staphylococci in 50 cells in a preparation in which one of the human sera was used; and later a curve was constructed in which the indices were obtained by dividing the number of bacteria in 50 cells in the rabbit's serum by the average number of bacteria contained in three counts of 50 cells each in the three human sera. A comparison of these two curves brings out no new points; they differ somewhat, but there are just as great variations in the curve based on

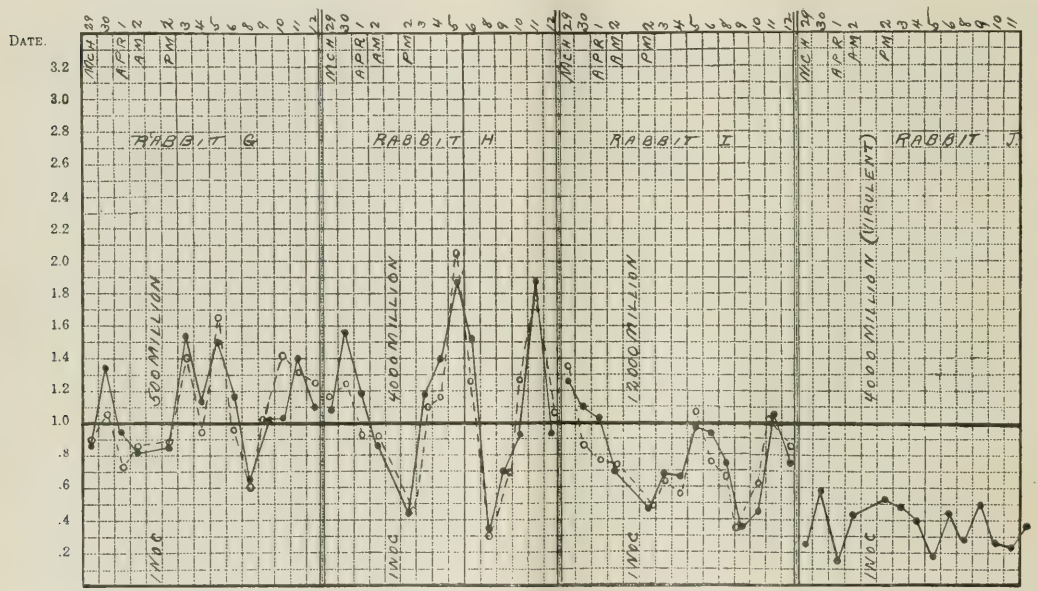
cutaneously, rabbit G receiving 500 million staphylococci from a vaccine prepared from the attenuated culture, rabbit H 4000 million staphylococci of the same vaccine, and rabbit J 12,000 million of the same. Rabbit I was given 4000 million of a vaccine prepared from the staphylococcus which had been passed repeatedly through mice.

In this series, as in the previous experiments, the indices varied in an apparently lawless way, and it seems unsafe to attempt to draw deductions from them.

Chart No. 4 shows the curves obtained for these four rabbits. The solid dots represent the indices obtained when only one of the three normal human sera was used as the basis of comparison, and the hollow dots the curve calculated on a basis of the average of the three normal human sera.

Parallel tests, as far as possible under exactly identical con-

Chart No. 4.



Solid dots show rabbits' indices referred to one of the normal sera. Hollow dots show rabbits' indices referred to the average of the three normal human sera.

the average of the three normal sera as in that based on only one, so that the first curve alone will be discussed.

In the first place during the period before inoculation the variations in the index for the different rabbits were as follows: Rabbit G, 0.81 to 1.34; rabbit H, 0.87 to 1.57; rabbit I, 0.70 to 1.26; rabbit J, 0.14 to 0.59. During the same period the variation of two of the normal human sera as compared to the third, the third being that used in determining the indices for the rabbits, was 0.70 to 1.66 in the case of one and 0.84 to 1.95 in the case of the other. After these preliminary observations, all of the rabbits were inoculated subditions, were made on the three normal human sera. The curves obtained by calculating the indices for two of these as tested against the third are shown in Chart No. 5.

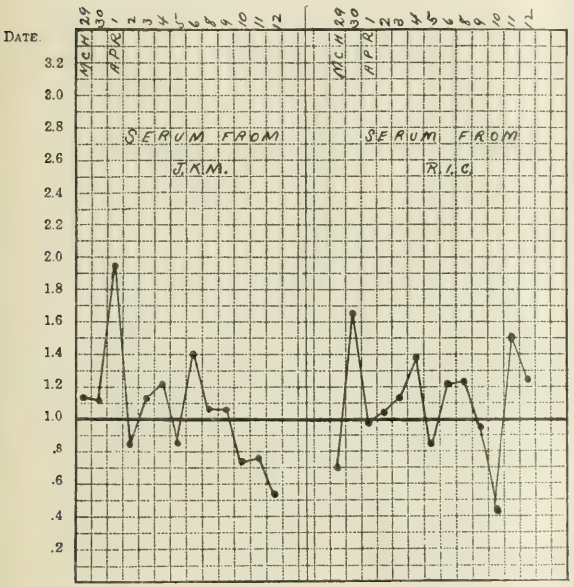
These curves are most irregular. In 13 observations one varies between limits of 0.52 and 1.95, the other between 0.42 and 1.66.

We do not expect the index to exhibit much wider variations under pathological conditions than these three normal sera show. Hence if the above results are trustworthy it would not seem possible to make use of the opsonic index as a means of diagnosis or as an indication for the treatment by

vaccine. No attempt will be made here to discuss the clinical value of the vaccine treatment. The existence of opsonin and the fact that it plays a part in phagocytosis seems well established, but we think it remains to be proven that it plays any part in immunity, or that it can be used as a means of diagnosis or as an indication for treatment.

If the normal serum varies in its opsonic content through as wide limits as pathological serum does, no amount of smoothing out these variations by pooling or striking aver-

CHART NO. 5.



ages will enable us to say that one opsonic index indicates infection or immunity while another does not.

In view of the discordant results obtained in the above experiments it seemed wise to determine if they might be due to personal error on the part of the observer. Accordingly a series of comparative tests were arranged to be carried out by three observers simultaneously, and as far as possible under exactly the same conditions, all these workers having had considerable experience with the technique.

For this purpose each of the three observers prepared three specimens of his own serum. These were given to a fourth man, who numbered them and kept a record of their source, so that the observer might not know with which serum he was dealing in a given test, until all the tests were made and the results obtained. An emulsion of fresh leucocytes and one of a 24-hour agar culture of Staphylococcus aureus was prepared, great care being taken to secure homogeneous emulsions, and, in the case of the bacterial, free from clumps. As soon as these were ready each emulsion was apportioned equally between each of the three observers, who immediately set to work putting up one preparation from each of the nine specimens of serum. Thus there were 27 preparations made in all on sera from three normal individuals.

The preparations were each incubated 15 minutes at 37° C. Spreads were made, stained with Hasting's stain, and 50 leucocytes and their contained bacteria were counted on each slide.

The results are shown in the accompanying Table No. 3.

TABLE NO. 3.

April 13, 1907.				Average.	Difference between highest and lowest counts.	Greatest absolute and percentage variation from average counts.
	C's serum.					
	1	2	3			
A's counts.....	238	224	197	219	41	19 or 8.6%
B's "	164	185	264	206	100	58 or 28%
C's "	241	252	177	223	75	46 or 20%
	B's serum.					
	4	5	6			
A's counts.....	196	203	255	218	59	37 or 17%
B's "	340	310	234	295	106	61 or 21%
C's "	189	319	211	273	130	84 or 30%
	A's serum.					
	7	8	9			
A's counts...	216	217	236	223	20	13 or 5.8%
B's "	213	211	291	238	80	53 or 22.4%
C's "	289	215	178	227	111	62 or 27.3%

Attention must be drawn to several points in this experiment. First we are dealing with three different sera which may contain different amounts of opsonin. In the second place, we have three different observer's results on the same serum, and here may be introduced personal differences, which, while they may be constant for each man and so not affect a comparison of his own results at one time with his results at another, would introduce an error in comparing his results directly with those of another observer. Thirdly, we have three observations by one observer on one serum.

Perhaps it is best to begin our examination of the results of this test by considering the third point first. The greatest variation between the three counts by any one man on one serum was C's counts on B's serum. His highest count was 319, lowest count was 189, a difference of 130. The greatest absolute and percentage variation from the average of his three counts on B's serum being 84 or 30 per cent.

The smallest variation between the three counts of any one man on one serum was A's count on A's serum, in which the highest and lowest counts were 236 and 216, respectively, a difference of 20; the greatest absolute and percentage variation from the average of his three counts being 13, or 5.8 per cent. It is evident from a comparison of these figures and from subsequent work done that a considerable error results from counting too few cells, 50 cells not being a sufficient number to yield a true average.

For the reason stated above (variation due to personal differences in making the counts) it does not seem wise to attempt any comparison between the results of the different ob-

server's observations on the same serum, although in this experiment they come out fairly close together, except in the case of B's serum, in which A finds the low average of 218 while B finds the high average of 296. The difference between individuals in these observations on the same serum in subsequent tests were much greater.

We now will consider the first point, namely, the differences between the three sera used, and here again it is perhaps not wise to consider the averages of the three different observers for the three different sera, but compare the averages of one observer on the three sera. Thus A's averages for the three sera are very close, 218 to 223, while B's varied from 206 to 295.

This experiment was repeated on the following day, using a much thicker bacterial emulsion. The results are shown in Table No. 4. Here a striking difference is noted between the results gotten by the different observers on the same serum.

TABLE No. 4.

April 14, 1907.				Average.	Difference between highest and lowest counts.	Greatest absolute and percentage variation between highest or lowest and average counts.
	C's serum.					
	5	6	8			
A's counts	921	931	943	932	22	11 or 1.1%
B's "	515	621	557	564	106	57 or 10%
C's "	647	548	603	599	99	48 or 8%
	B's serum.					
	2	3	7			
A's counts	941	903	1023	956	120	67 or 7%
B's "	465	521	975	720	454	255 or 35%
C's "	725	750	609	695	141	84 or 12%
	A's serum.					
	1	4	9			
A's counts	903	946	935	928	43	25 or 2.7%
B's "	651	790	697	713	139	77 or 10%
C's "	813	728	463	668	350	205 or 30%

The thicker emulsion makes counting very much more laborious, but probably yields more accurate results, provided the emulsion used is not so thick as to introduce error by causing bacteria to overlie leucocytes without being really in them, or causing the number in the leucocytes to be so great as to render accurate counting impossible.

After each of the previous tests were made the slides were given to a fourth man who kept record of them, but renumbered them, and after mixing them up, issued them again to the different observers who made recounts.

On the recounts of the slides of the first experiment, differences varying from 1 to 69 were made on the individual slide, with an average difference for the 27 slides of 29. The recounts on the slides of the second test showed considerably greater absolute variations, but perhaps the percentage variation was not much greater, as the bacterial emulsion used in the second test was much thicker, and we are therefore dealing with much larger numbers.

Further tests were performed in which from six to nine preparations each were made from one serum, the bacteria contained in 50 cells being enumerated on each preparation. The results will not be detailed here, but they strengthened the conviction that the present technique is inadequate. The problem now was to find out in what points the error lies. Not much more than a start has been made along that line, but it seems worth while to state what has been done and indicate the lines along which further investigation might be made, hoping that those who are working in opsonins will at least test their technique, and, if it is found deficient, be saved from wasting further time on a method which yields only inaccurate results.

That phagocytosis faithfully follows definite laws seems probable. That opsonin exists and plays a part in phagocytosis we are equally agreed. That many factors influence phagocytosis we are certain. Whether we can control enough of these factors to study the process in an exact and scientific way may be open to question.

An effort was made to control as many of the factors influencing phagocytosis as possible in the following tests.

Fresh leucocytes were washed and great care was taken to get a homogeneous emulsion. The same care was resorted to in the preparation of the bacterial emulsion. A very fine capillary pipette was used to reduce as much as possible the effect of settling of the bacteria and leucocytes during incubation; the serum, bacterial, and leucocytic emulsions, in equal parts, were mixed very thoroughly before incubating and again after incubating before making the spreads for counting. Light staining was used in order that all the bacteria within a cell, even those overlying the nucleus, could be counted, and then a number of counts of 50 cells each was made on *one* slide. It seemed that if these counts all made on the same slide varied greatly that the technique certainly could not be applied to the investigation of different preparations in which the number of variable factors could not possibly be as small as in this one preparation.

The results of 12 counts of 50 cells each made on one slide will illustrate what we found. They were: 331, 422, 391, 388, 287, 367, 412, 489, 418, 495, 371, 503 given in the order in which they were made, beginning away from the end of the smear and counting down to the end.

It seems quite evident from a comparison of these 12 counts that 50 cells do not suffice to give us a true idea of the averages. In these 12 counts we have a variation of from 287 to 503.

An attempt was made to get an idea of how many cells one would have to count to find a true average, and for this purpose these 12 counts were combined in groups of 100, 150, 200, and 300. The averages for these different groups are given on a basis of the content of 50 cells, as this furnishes a convenient means of comparison.

The averages for the six groups of 100 cells each are as follows: 377, 389, 327, 450, 457, 437. For the four groups of 150 cells each the counts are 381, 347, 439, and 456. For groups of 200 each the counts are 383, 388, 447. For groups of 300 each the counts are 364 and 448. The

average for the 600 cells is 406, and we are probably justified in assuming that this represents more closely the true average than any of the smaller groups. On this assumption let us calculate the greatest absolute and percentage variation in each of the smaller groups. In the groups of 50 each this greatest variation from the average for the 12 counts is 406 — 287 = 119, or 26 per cent. In groups of 100 each it is 79, or 19 per cent; in groups of 150 each, it is 59, or 14+ per cent; in groups of 200 each it is 41, or 10 per cent; in groups of 300 each it is 42, or 10 per cent. As far as the result of this one test goes it shows that we can reduce the error by counting larger numbers of cells, but that we still have an error of, in this case, at least 10 per cent, in counting as many as 300 cells.

The impression prevailed among the men in the laboratory that the count was dependent in part upon the place on the slide from which the cells were counted, although there was difference of opinion as to where the counts would be greatest. The counts just described seemed to throw some light on this question, as the counts were begun some distance back from the end of the smear, and were continued moving toward the end. An examination of the counts shows in general that the highest counts occurred toward the end of the slide, particularly is this evident if the larger groups are considered.

There seems a probable explanation for this. The smears were made in the way familiar to all, of putting a drop of the mixture from the pipette near one end of a slide and with the end of another slide, held at an angle to the first, drawing the fluid along the length of the slide. There is a distinct sorting out process of the cells by this method, the smaller ones being the first to slip from under the end of the second slide and remaining behind on the first slide. Thus, in examining such a preparation one usually comes first to the lymphocytes, and though the sorting out process is not so effectual among the large mononuclears and polymorphonuclears, it is evident to some extent here also.

It seems possible that those polymorphonuclears containing a large number of bacteria may be so increased in bulk or consistence as to be spread out on the slide at a different place from those containing fewer bacteria. In order to discover if this might be true slides were divided into different zones and counts of 150 cells made in each of these zones.

The zones were 1 cm. wide and the results of the counts on two slides so determined, in connection with the 12 counts on one slide referred to above, indicate that counts made near the end of smears are slightly larger than those made near the beginning.

The results for 150 cells in each zone were as follows:

	a	b	c	d
Slide No. I.....	454	484	484	
Slide No. II.....	288	306	362	404

To summarize briefly the conclusions which these experiments seem to justify:

1. No high degree of opsonic immunity such as is possible in antitoxic and bactericidal immunity, can be produced in rabbits by ordinary inoculation procedures with Staphylococcus aureus.

2. None of the present methods of estimating the opsonic content of the blood seem sufficiently accurate to be of practical value.

It seems important that further effort should be expended in finding a reliable technique for clinical purposes rather than in continuing to pile up statistics which are so inaccurate as to be misleading.

THE OPSONINS IN TYPHOID IMMUNITY.

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Through the discovery of opsonins new protective bodies have been found, which apparently are of great importance in immunization against infectious diseases, and it is therefore interesting to determine to what degree these bodies are active in typhoid fever in which the agglutinins and bactericidal substances form in large amounts. He who believes in a purely humoral typhoid immunity, and holds the opinion that in the body fluids of typhoid patients bactericidal substances develop in sufficient quantity to kill the bacteria without the agency of phagocytes, might expect that opsonins, which prepare bacteria for phagocytosis, would be of less or no importance in typhoid immunity. The rôle, however, which agglutinins and bactericidal substances play in typhoid immunity is doubtful. All attempts to make a prognosis in typhoid from the development of these bodies must be considered unreliable. The numerous observations of Jörgensen[1] show that the agglutinating power usually declines after the third week. A high agglutinative power does not at all protect against relapses or recurrences; and the same may be said of the bactericidal substances, if determined by the Neisser[2] method. Stern and Korte[3] report that in a patient whose serum revealed the highest bactericidal titre (1:4000000) ever observed by them, a relapse developed eight days later. Other authors also have observed that a blood of high bactericidal power does not protect against recurrence. The bactericidal substances, as demonstrated by the Neisser method, diminish like the agglutinins

[1] Centralbl. f. Bakteriol. u. Parasitenk., Jena, 1905, XXXVIII, 1 Abt., 475.

[2] Berl. klin. Wchnchr., 1904, XLI, 213.

[3] Ibid.

towards the end of the disease, and especially in convalescence.[4,5] But this refers only to the bactericidal action *in vitro*. Other results were obtained if the bactericidal power was measured by the Pfeiffer method. Töpfer and Jaffé[6] comparing the bactericidal power *in vivo* and *in vitro*, in a large number of typhoid patients and immunized animals, obtained very surprising results. Working with the Neisser method, they found, like Stern and Korte, a high bactericidal power during the active stage of typhoid, and a weaker one during convalescence. But with the Pfeiffer method they found that the serum of convalescents was more effective than that of acutely ill typhoid patients. Immunized animals never showed *in vitro* such high bactericidal power as typhoid patients; tested by the Pfeiffer experiment it was the reverse. The authors do not explain this; they only express their belief that it is not due to differences in the active bactericidal substances.

Little study has been made hitherto of the typhoid opsonins. Wright and Douglas found the typhoid bacillus "eminently unsusceptible" to the opsonic action of the blood fluids. On the other hand, Leishman, Harrison, Smallman, and Tulloch[7] decided from their work that, if typhoid opsonins existed, their presence could not be demonstrated by the method they adopted. They found no changes in the opsonic power during the course of the immunizing process. Hektoen[8] mentions that in typhoid convalescents the opsonins are greatly increased, and that the opsonic index often reaches as high as four.

If it is true that the typhoid opsonins only develop to a marked degree during convalescence, then the results of Töpfer and Jaffé may possibly be explained by the fact that in the Pfeiffer experiment they injected immune opsonins and thereby caused a much more active phagocytosis, which determined the survival of the animal. In favor of this explanation are the experiments of Besredki,[9] who injected typhoid immune serum with typhoid bacilli into the peritoneal cavity and observed an increased phagocytosis which, however, he thought was due to the action of stimulins. Töpfer and Jaffé found also a stronger extracellular bacteriolysis in the exudate of highly immunized animals. But this may be explained by the fact that, if there is a stronger phagocytosis, a smaller number of bacteria outside the cells are exposed to the influence of the bactericidal substances; and a smaller number of bacteria are more readily killed by these substances than a larger one.

It was my intention to contribute to the solution of these questions by the simultaneous observation of agglutinins and the bactericidal and opsonic powers of the serum in several cases of typhoid fever. But because of lack of time, I have confined myself to experiments with immunized rabbits. I also counted the leucocytes to look for relations between the humoral and leucocytic reactions, and to determine whether there occur in the immunized rabbit changes in the blood picture similar to those observed in cases of human typhoid fever.

Agglutination was tested by the macroscopic method with the usual precautions. The result was determined after one hour's incubation. For the bactericidal power Wright's method was first tried, but the results were very inconstant. That this is due to the method is obvious from the fact that Wright[10] himself gets very contradictory results. He, for instance, examined the same healthy man twice and found the first time a bactericidal power of 3120 (the serum killed 3120 bacteria in 24 hours), while the second time he obtained a value of 6,000,000. Besides he does not consider in his method the possibility of diversion of complement. In order to complement the whole amount of amboceptors in a typhoid serum, it is often necessary to add more than a hundred times as much normal serum, and consequently, using Wright's method, I had to work with a serum at least 100 times diluted, and in order to discover smaller values, I had to resort to special experiments without adding complement. Leishman and his co-workers also do not consider the possibility of diversion of complement. This is a great error, since numerous experiments (Neisser and Wechsburg,[11] Töpfer and Jaffé,[12] Korte and Steinberg[13]) have shown that in high immune sera there is rarely present a sufficient amount of complement to satisfy the amboceptors attached to the bacteria, and to produce thereby the bactericidal effect. Highly immune sera without addition of complement very often have no bactericidal power at all.

It is hardly probable that what has almost always been observed by German and French investigators, should never have been found by Leishman and his co-workers. And if we submit the curves of these authors to a closer analysis we find that in all probability the Neisser-Wechsburg phenomenon was present. On the seventh to the ninth day after the first inoculation there was a distinct increase of bactericidal substances. The second inoculation was performed on the eleventh day. The effect was a more rapid rise of the bactericidal curve. But three days later there begins a sudden, steady decrease to a subnormal value; then the curve rises again to higher values. The authors are unable to account for this, and yet a diversion of complement would offer a full explanation. The fall of the curve four days after the second inoculation is probably not to be explained by a decrease of bactericidal substances. On the contrary it is probably due to a marked production of amboceptors, so that more and more complement is bound to that portion of the amboceptors not attached to bacteria.

I have considered these results of Leishman fully in order to demonstrate the weakness of Wright's method in its present form. The simplicity also of the latter's method is only apparent. I found that I could work very much faster with

[4] Berl. klin. Wchnschr., 1904, XLI, 213.
[5] Korte and Steinberg. Deutsches Arch. f. klin. Med., Leipz., 1905, LXXXII, 321.
[6] Ztschr. f. Hyg. u. Infectionskrankh., Leipz., 1906, LII, 393.
[7] J. Hyg., Cambridge, 1905, V, 380.
[8] J. Am. M. Ass., Chicago, 1906, XLVI, 1407.
[9] Ann. de l'Inst. Pasteur, 1901, XV, 209.
[10] Proc. Roy. Soc. Lond., 1903, LXXI, 54.
[11] München med. Wchnschr., 1901, XLVIII, 697.
[12] Ztschr. f. Hyg. u. Infectionsk., Leipz., 1906, LII, 393.
[13] Berl. klin. Wochenschr., 1904.

the Neisser method, as modified by Stern and Korte for the sero-diagnosis of typhoid fever. More important still, this method leads to more exact results. In this method to a constant mixture of bacteria and fresh serum (complement) there is added inactivated typhoid serum in varying quantities As a measure of the amboceptors present, I took that dilution of the serum, which after three hours' exposure at 38° C. produces a definite decrease of the colonies as compared with the effects produced by the fresh normal serum. To meet the objection that the results obtained by this method might be due to agglutination alone, it may be said that these two reactions often do not run parallel, and that the serum frequently exhibits bactericidal powers in much higher dilutions than it does agglutinating. The simplest proof against this objection, in my opinion, can be obtained by the following control test, in which heated serum without complement is added to the bacteria. The agglutinins are not destroyed by the process of inactivation, and their effect in the original experiment cannot be stronger than in this control test. In my experiments I have used frequently such a control test with a serum dilution of 1:10, and I have observed only a very slight diminution of colonies as compared with the agglutination power. The effect of the agglutinins on the number of colonies was less than the influence of the normal serum, in a dilution of 1:15, which was used as complement. This may be explained by the fact that after the agglutinins have been absorbed by the bacteria, the new generations of bacteria may develop without being agglutinated.

Practically the technique as described by Stern and Korte was used, but I found two slight modifications advantageous. First, I did not make the dilutions of the bacteria with broth, but with normal salt solution. The reason for this is that the bacteria when transferred to new broth, develop rather quickly even at room temperature, and therefore irregularities in the number of inoculated bacteria may occur. In order to obtain an equal quantity of broth in each tube the dilutions of the normal serum were made with broth. Second, I inoculated the tubes with a smaller amount of bacteria, in order to have all the bacteria more quickly killed, instead of causing mere reduction in their number. I used 0.1 cc. of a 24-hour broth culture, dilution 1 to 8000. In the whole series of experiments, but one broth, all made at the same time, was employed. The mixture was made in long test tubes, and before plating, the agar was poured into them. The tubes were then carefully shaken and the contents poured into the plating dishes.

Greater difficulties were found in the determination of the *opsonic power.* The typhoid bacillus, after being taken up by the leucocyte, is very quickly digested. Even after a very short time of incubation (for instance, five minutes), bacteria in all stages of digestion are seen, from the well stained, clearly outlined bacillus to a hardly visible, pale shadow (Hastings' modification of Jenner stain). Therefore, in determining the phagocytic index, the question arises, how many bacteria may be already digested and consequently invisible? Because of this fact, it must be expected that a comparative count of phagocyted typhoid bacilli can not be attempted without considerable error. One might hope to reduce these errors by a shorter incubation time. However, that would not be advisable in the determination of the opsonic index, since due to slight differences in the diameter of the capillary pipettes, unequal heating would follow if the incubation time were too short. In order to avoid these disadvantages, it was very natural to apply an analogous method to that used for the determination of agglutinins, namely, to determine *in what degree of dilution the serum ceases to cause phagocytosis.* By this method very definite results were obtained. Of course, as in all absolute measurements, some precautions must be carefully observed. First, the choice of the test-bacillus is of great importance. As shown by Löhlein,[14] the individual qualities of a given strain are of marked influence on the resulting phagocytosis, and on the action of opsonins. Löhlein, for instance, found among three different strains of B. coli one that was opsonized very readily; the other two were but little influenced by normal serum. One of them was very susceptible to phagocytosis, without any opsonic action by the serum; the other one was not taken up at all, even under the influence of serum. According to Löhlein the virulent bacteria generally have the greatest resistance to phagocytosis.

In order to get good results with the above-mentioned dilution method, it is best to use a strain which is not susceptible to phagocytosis without preparation by opsonins. The typhoid strain used by me for the opsonin test was of this kind. It was grown directly from the blood of a typhoid patient. In normal salt solution, as well as in the highest dilutions of the serum, there was no phagocytosis at all, or only an average of one-half to one and a half bacilli per leucocyte. However, as it would be necessary with such a small degree of phagocytosis to count a very large number of leucocytes in order to obtain accurate results, I took as measure of the opsonic power, the dilution in which the number of phagocyted bacteria surpassed 0.5 per cell. When a bacillus is used which is susceptible to spontaneous phagocytosis, a control test with salt solution must always be made. The measure of the opsonic power is then that dilution in which phagocytosis considerably exceeds spontaneous phagocytosis. Usually I made the test in dilutions of 1:2, 1:4, 1:8, and so on. Several times I have examined in this way the serum of three normal rabbits. In these cases the phagocytosis nearly always dropped below 0.5 per cell when a serum dilution of 1:16 was used. In a dilution of 1:8 the phagocytosis just surpassed 0.5 per cell. As in making this test there occurs a further three-fold dilution by adding equal quantities of bacterial emulsion and leucocytes, the expression of opsonic power is 24.

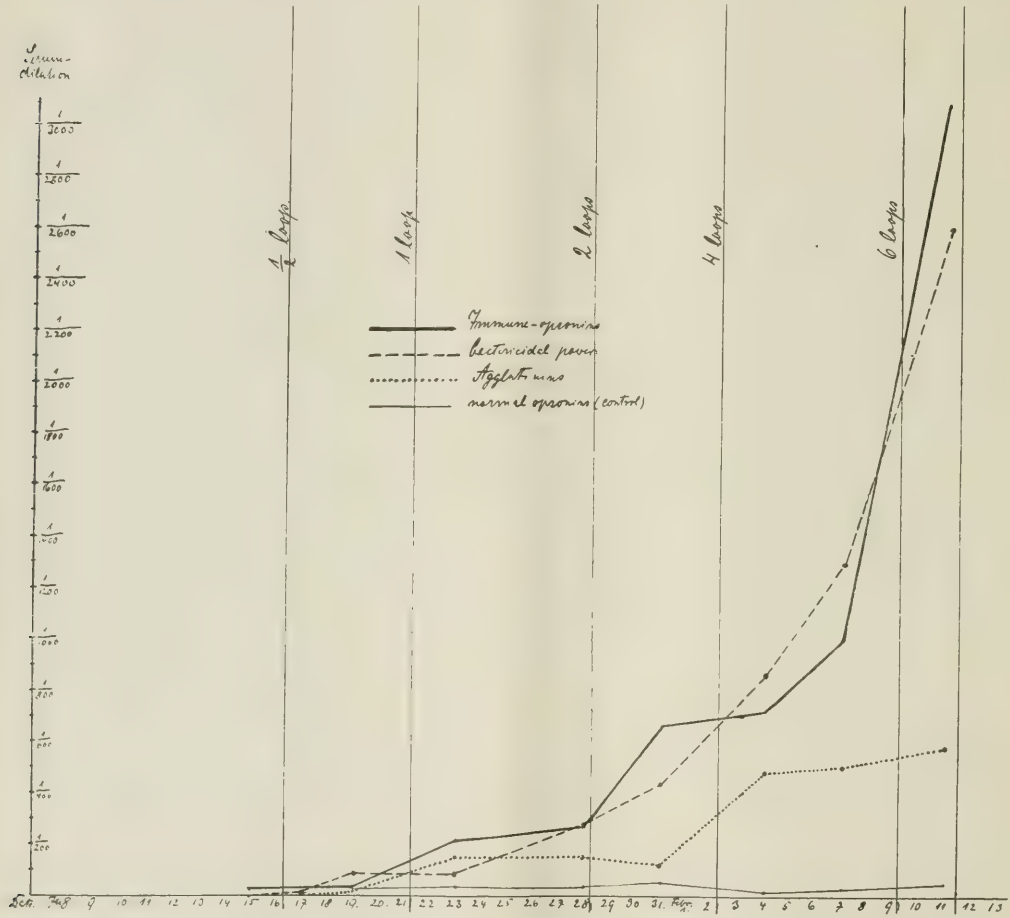
The influence of the number of bacteria used in the opsonin test is important. Apparently in a given culture the bacteria differ in the readiness with which they are opsonized, some being easily opsonized, others only with very great difficulty. The normal opsonins are only able to opsonize the

[14] Ann. de l'Inst. Pasteur, 1906.

susceptible organisms. As the opsonic power becomes higher, more resistant bacteria are opsonized.

To obtain accurate results with the dilution method it is necessary to employ rather thick bacterial emulsions of constant density. I found it convenient to use a suspension of three loops of a 24-hour agar culture in 1 cc. salt solution. It is advisable to control the degree of concentration by a standard emulsion. The incubation time in my experiments was 10 minutes; however, 5 minutes would possibly be bacteria are distributed among a larger number of leucocytes. However, this influence does not seem to be very considerable, as is shown by the following experiment: To two tubes, equal parts of bacterial emulsion and leucocytes were added, but in one of them the leucocytic emulsion had been diluted 10 times. Each leucocyte from this tube contained 21.6 bacteria; from the first one, 11.6 bacteria.

The curve below shows the development of the opsonins, the agglutinins and the bactericidal substances under the influence of increasing doses of living typhoid bacilli, subcutaneously injected.



better. The blood was taken every morning between 11 and 12 o'clock, before the rabbit had taken any food. At the same time the blood count was made.

The number of the leucocytes may have a certain influence on the result. If a given number of opsonized bacteria are mixed with a small number of leucocytes every leucocyte will take up more bacteria than if the same number of opsonized

This curve was constructed in the following manner: As a measure of the opsonic power, not only the highest dilution in which the phagocytosis just surpassed 0.5 was taken but a more accurate determination was attempted in the following way: If the degree of the first positive phagocytosis was

just about 0.5, the corresponding dilution itself was taken as a measure of the opsonic power. If, however, the first positive phagocytosis was considerably higher than 0.5, the value was considered nearer to the next higher dilution. How that is expressed in the curve is best shown by an instance.

On January 31 and on February 4 the highest dilution showing positive phagocytosis was 1:384. But the phagocytic index in this dilution was very different in the two cases. On January 31 there was 0.66 bacterium per leucocyte, on February 4, 4.2. On February 4, therefore, the opsonic power was considerably higher than on January 31. The phagocytic index in the next higher dilution was but a little less than 0.5, namely, 0.42. For measuring the opsonic power, it was now calculated what percentage of 0.5 the phagocytic index was in the first dilution in which it was less than 0.5. The corresponding percentage of the difference between the last dilution with positive phagocytosis and the first dilution with negative phagocytosis was added to the last dilution with positive phagocytosis, and the number so obtained was taken as an expression of the phagocytic power. In the above-mentioned instance the determination was done in this way:

The phagocytic index in dilution $1/384 = 4.2$
The phagocytic index in dilution $1/768 = 0.42$
$0.42 = 84\%$ of 0.5
84% of $384 = 323$
Therefore the opsonic power $= (384 + 323) = 707$.

I realize that these figures are not accurate, but represent in a general way the increase of the amount of opsonins in the serum.

In constructing the curve of bactericidal power, it was not possible to rectify the values in a similar manner. However, I tried to express in my curve whether the first clear reduction of colonies was relatively slight or marked. In the case of a slight reduction, the corresponding dilution itself was taken as the expression of the bactericidal power. In the case of a very strong reduction the middle point between the corresponding dilution and the next higher dilution was taken.

Since in the arrangement of my experiments, 0.5 cc. complement and 0.1 cc. bacterial emulsion were always added to 1.0 cc. of the diluted serum, the number representing the degree of serum dilution must still be multiplied by 1.6 in order to get the real value of the bactericidal power.

The curve (page 248) shows that at the beginning of immunization the three protective substances increased at about the same rate. Later there was a rapid increase in the opsonic and bactericidal power, but only a *very* slight increase in the development of agglutinating substances. It is very striking that the dilutions in which the first increase of opsonic and bactericidal effect is found are nearly the same. The average ratio between the dilutions in which opsonic and bactericidal action ceased was $\frac{1.04}{1}$.

However, in comparing the absolute values, it must be remembered that the opsonins were determined after an incubation of ten minutes, the amboceptors after three hours, and the agglutinins after one hour.

By these experiments it has been shown that by *immunizing a rabbit against typhoid, opsonins are formed in a considerably high degree.* When we take into consideration the fact that the opsonic effect was obtained in ten minutes, we may suppose that the opsonins may be the most active substances of the typhoid immune serum. Therefore, it is possible *that the preparation of bacteria for phagocytosis, and the phagocytosis itself, may be at least as important for immunization against typhoid as the increase of bactericidal action of the blood serum,* which by many is now considered the most important factor.

The fine line of the curve shows the opsonic power of the serum of a normal rabbit, which was always examined as a control at the same time and in the same way as the immune serum. There occur only slight oscillations. Even these oscillations, however, are apparently only physiological variations of the opsonic power of the normal blood. The fact that corresponding oscillations are to be seen in the curve of the immune opsonins shows that these variations depend chiefly, if not entirely, upon irregularities of the technique. Therefore, the curve of the immune opsonins should probably have a more regular course and coincide still more closely with the amboceptor curve.

In spite of the high amount of opsonin present, the *opsonic index* examined by the original method of Wright (with a thin bacterial emulsion) on repeated examinations always showed a low value: On January 4, 1.65; on January 7, 1.04; on January 11, 0.82.

This seems to show *that the opsonic index as determined by the Wright method cannot be a measure of the opsonic power of a typhoid immune serum, at least not in the higher grades of immunity.* The index seems to rise with the first development of immunity; with the further development of immunity, it drops. I can find no other explanation for this than the fact *that the amboceptor laden bacteria are much more quickly digested by the leucocytes,* and thereby become invisible. Leishman and his co-workers, who also found a low phagocytic index in the sera of typhoid patients, tried to explain it by an intracellular bacteriolytic action of the serum. This explanation cannot be accepted in my experiments, because very numerous bacteria, staining normally, were always seen outside of the cells, and because *destruction of the complement by heat had no influence on the phagocytic index.*

During the first days after the injection of bacteria, *a more or less marked leucocytosis occurred.* It was due chiefly to an increase of the polymorphonuclear neutrophilic cells. I did not find an increase of the large mononuclear leucocytes, as is so often found in typhoid fever.[15] The eosino-

[15] Thayer: Johns Hopkins Hosp. Reps., Balto., 1900, VIII, 487.

philic cells likewise did not show any considerable variation in number.

CHART I.

Injections of living typhoid bacilli.	Date.	Agglutination.	Bactericidal power.	Opsonic power.	Normal opsonic power of control.	Index of Wright.	Leucocytes, total.	Polymorph. neutrophiles absolute number).	Mononuclears.
	Jan. 8		<16 *						
	" 9		<16 *						
	" 12						8000	2600	5000
	" 13		<16 *				8500	2800	4900
	" 14						8600	2800	5300
	" 15	5	<16 *	<30					
½ loop	" 16	5					8400		
	" 17	5	>16				10900	6900	3900
	" 18						14700		
1 loop	" 19	>10	96	34	24		8800		
	" 23	160	96	204	43		25400	16300	9300
2 loops	" 28	160	288	284	40		9300	4400	4300
4 loops	" 31	120	432	669	52		12700		
	Feb. 4	480	864	708	10	1.65	11600		
6 loops	" 7	500	1296	999	29	1.04	9700	3900	5300
	" 11	575	2592	3072	58	0.82			

* Probably = 0, as 1:16 was the lowest dilution (for the curve taken as = 0)
The double black lines correspond to the injections of bacteria.

Because of the high amount of opsonin in the immune serum, it was easy to study the peculiar qualities of these opsonins. First, I was able to show that the typhoid immune opsonins are thermostabile, resisting heating to 55-58° C. for half an hour. The average numbers of bacteria contained in a leucocyte are shown in Table I.

TABLE I.

	With unheated serum	With heated serum.
Dilution 1/48	∞	∞ *
Dilution 1/192	2.87	2.32
Dilution 1/768	0.63	0.53
Dilution 1/3072.....	0.21	0.06

Salt solution, 0.15.

* Leucocytes crowded with bacteria in all stages of bacteriolysis.

According to this table, the opsonic action disappeared in the same dilutions of the heated and unheated serum, and was of an equal power in corresponding dilutions. On the contrary, the opsonin of the normal serum was thermolabile under the same conditions.

TABLE II.

	Unheated serum.	Heated serum.
Dilution 1/1	..	1.12
Dilution 1/6	14.3	1.18
Dilution 1/12	4.7	0.2
Dilution 1/24	0.65	0.04
Dilution 1/48	0.2	0.05

Salt solution, 0.0; (70 cells).

However, the table shows that the opsonin of the normal serum does not disappear entirely after heating for half an hour to 56° to 58° C. Whether this small amount of thermostabile opsonin is identical with the thermostabile immune opsonin, cannot be decided until further experiments have been made. These experiments were repeated with the same results.

In order to find out whether the typhoid immune opsonin is specific or not, the opsonic index of the immune serum for other bacteria was first determined. Next I tried to absorb the immune opsonin by saturation with other bacteria. The opsonic index for other bacteria was also determined, not only with an unheated normal serum, but also with a heated one. By determining the index with heated sera, nonspecific action of the typhoid immune opsonin can apparently be shown much better, because of the thermostability of the immune opsonin. The results are given in the following table:

TABLE III.

Phagocytic Index.	Typhoid immune serum.		Normal serum.	
	Unheated.	Heated.	Unheated.	Heated.
Against Staphylococcus aureus	7.5	0.63	6.7	0.51
Against Streptococcus..	6.2	2.4	6.7	1.8
Against Bacillus tuberculosis *	1.9	0.2	1.9	0.29
Against guinea pig erythrocytes	Traces		Traces	

* These specimens were kindly made by Mr. Sellards.

The typhoid immune serum had no higher opsonic power for the other organisms tested than had normal serum, and by heating, this opsonic power was destroyed in the same degree as the opsonic power of the normal serum. Therefore, it is evident that *the typhoid immune opsonin is specific,* at least against the organisms studied. Also, human erythrocytes were not opsonified by the immune serum in a higher degree than by normal rabbit serum.

By saturation with some other micro-organism no immune opsonin could be absorbed. The phagocytic index of the immune serum against typhoid bacilli was:

	Before saturation with staphylococci.	After saturation with staphylococci.
In a dilution of 1:243.....	7.2	7.4

Also by saturation with guinea pig corpuscles the opsonic power of the immune serum for typhoid bacilli was not diminished.

Contrary to the immune opsonin, *the opsonin of the normal rabbit serum proved to be largely non-specific.*

In order to determine to what degree the normal opsonin can be absorbed, it is necessary to use very large quantities of bacteria and a concentrated serum. With this purpose, several agar cultures were emulsified in a few drops of normal salt solution. It is necessary, of course, to employ a strain easily opsonized. This suspension was mixed with an equal part of normal rabbit serum and drawn into capillary

pipettes. These were sealed and incubated for some time; in the first experiment for fifteen hours, in the second one for three and three-quarters hours. At the same time the part of the serum which was to be used for the control was also sealed in a capillary pipette and incubated. Then the staphylococci were removed. In the first experiment they were thrown down by the centrifuge, in the second they were filtered out by a very small Berkfeld filter. Then the opsonic index of the clear fluid was tested. In the first experiment there were still some staphylococci in the clear fluid. However, there was no trouble in distinguishing the typhoid bacilli and staphylococci within the leucocytes. Some doubtful organisms were taken for altered typhoid bacilli. The phagocytic index was:

TABLE IV.

	Experiment I.	Experiment II.
With normal serum.....	5.9	3.9
After absorption with Streptococci..	0.23	0.09
With salt solution.....	0.17	0.09

As shown by this table, *the opsonin of the normal serum can be absorbed completely by other bacteria. Therefore the above-mentioned thermostabile opsonin of the normal serum is apparently not identical with the typhoid immune opsonin.* Table III also shows that in the typhoid serum there is *no increased production of opsonins for other bacteria in addition to the typhoid opsonin.* This possibility must be considered, as Hektoen[16] has shown the presence of hæmopsonins in cases of typhoid fever.

That the typhoid immune serum did not contain nonspecific stimulins is seen by the fact that the activity of the leucocytes toward other bacteria was in no degree favored by the typhoid serum. I mention this, because Leishman and his co-workers[17] claim to have induced a considerable production of stimulins by vaccination with typhoid bacilli. The first sentence of Leishman's description of his stimulin test shows why he was mistaken. He gives this definition of stimulins: "Substances which appear to stimulate phagocytosis, but differ from opsonins in being thermostabile." The more recent observers generally agree that the immune opsonins, which are identical with the "bacteriotropic substances" of Neufeld and Rimpau,[18] are thermostabile. It is, therefore, evident that Leishman and his co-workers really determined the amount of typhoid immune opsonin by their stimulin test.

I will not speak of all the possible reasons why Leishman failed to find an increase of opsonins following typhoid vaccination. The main cause, in my opinion, is that he used an old laboratory strain of bacteria, which apparently was little susceptible to opsonic action. However, I can only surmise this, because in Leishman's paper there is nothing said about the strain used in regard to its resistance to phagocytosis in normal salt solution.

The question arises whether the immune opsonin is formed by the transformation of the normal opsonin under the influence of the infection, or whether it is an entirely new substance. As the opsonic power of the typhoid serum for other bacteria is not reduced (*v.* Table III), and as furthermore the normal opsonins for typhoid bacilli and staphylococci are apparently identical, it must be concluded that *in the typhoid serum, in addition to the immune opsonins, the non-specific normal opsonins are present in normal quantities.* Therefore it is probable that the *immune opsonin* is not a transformation of the normal opsonin, but a *definitely new substance.*

Similar results to those quoted in the above experiments were obtained by Neufeld and Hühne. I am very sorry I did not see this paper of Neufeld and Hühne,[19] which was read in 1906 at a meeting of the "Freie Vereinigung für Biologie," until my experiments were finished and the greater part of this paper was written. I publish my paper in its original form, because I consider it important that different observers have independently obtained similar results, and because these results do not agree with those obtained by Leishman.[20]

Concerning the question whether the opsonins are different from other protective substances, my experiments do not offer much new evidence. However, there are some points of interest. In the highest dilutions in which an opsonic action could be found, no agglutination of bacteria was seen, even in the smears, and the phagocyted bacteria were distributed singly in the leucocytes. This cannot be considered conclusive evidence against the identity of agglutinins and opsonins, as the same substances which agglutinate the bacteria in a certain concentration might in a much higher dilution possibly be able to opsonify the bacteria. A more positive proof against this identity is given by the *different course of the curves of agglutinins and of opsonins.*

The parallel course of the opsonin and amboceptor curve is very striking, as is also the fact that both substances cease to be active in the same dilutions. And further, as both substances are thermostabile and specific, the suspicion arises that they may be identical. But even though this parallelism be a rule, it can not be considered a positive proof of the identity of these substances, as it is quite possible that two substances, which are apparently very similar and are produced under the same conditions, may be formed in equal quantities. Neufeld and Rimpau give some important reasons against this identity, but they acknowledge that a positive proof of non-identity has not yet been advanced, at least in the case of typhoid fever.

Finally, it must be asked whether these results can be useful for diagnosis. I have given my reasons why the index taken in the ordinary way cannot be considered a valuable method in typhoid fever. An examination with the above described dilution method requires too much time, though

[16] J. Am. M. Ass. Chicago, 1906, XLVI, 1407.

[17] L. c.

[18] Deutsche med. Wchnschr., 1904, XXX, 1458.

[19] Centralbl. f. Bakteriol., 1906, Bd. XXXVIII, Abtl., 27 Beil.

[20] Neufeld and Hühne's complete paper has just appeared in Arb. a. d. k. Gsndhtsamte., Berl., 1907, XXV, 164.

far less than the determination of the bactericidal power, which has been advised for diagnostic purposes.

I examined the opsonic power in only two cases of typhoid infection. The first one was a case of typhoid fever in about the seventh week. Here the serum in a dilution 1:120 caused a very marked phagocytosis, whereas the control serum in a dilution 1:30 caused less phagocytosis, and with the control serum diluted 60 times, there occurred no phagocytosis at all. The opsonic index was 1.02.

The second case was one of cystitis, due to a typhoid-like bacillus. The patient had had typhoid fever many years ago. The serum of this patient still caused a very marked phagocytosis in a dilution 1:288 (phagocytic index 4.8). Higher dilutions unfortunately were not made, because such a high opsonic power was not expected. The control serum caused but slight phagocytosis in a concentration of 1.36 (phagocytic index 0.66). The bacillus isolated from the urine had the cultural qualities of B. typhosus.

In my opinion it will be most advisable to study for diagnostic purposes the different effects of heating on the normal opsonins and the immune opsonins. As the normal serum contains only traces of thermostabile opsonins, it will be useful to look for them in a dilution of about 1:30. Perhaps it will be possible to differentiate the thermostabile opsonin of the normal serum from the immune opsonin, and to shorten the method by heating the serum for a shorter time and at a higher temperature.

With this method the differences between the normal and the typhoid serum must be very great. It will not be necessary to detect small differences in the number of the phagocytic bacteria, the determination of which takes too much time, and is open to so many opportunities for error.

STUDIES ON THE SPECIFICITY OF OPSONINS IN NORMAL AND IMMUNE SERUM.

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In the various papers of Wright and his collaborators to which I have had access, the question of specificity of the opsonins is nowhere discussed, though everywhere it is apparent that they consider the opsonins specific. This is very evident from the fact that they have used the opsonic index for diagnostic purposes, and as this would have no value unless the opsonins were specific, I think we may safely assume that they believe the question of specificity to be settled.

From the clinical results obtained by Wright and others by the administration of vaccines controlled by the opsonic index, it has seemed evident that the increase of opsonin present in the patient's serum is specifically related to the germ used. Moreover, according to Wright, the opsonic index to the organism causing the infection or used as a vaccine, is often abnormal, while with other organisms it varies very little from that of the control serum. On clinical grounds, therefore, the assumption of specificity of the opsonins would seem justified.

As this clinical method of arriving at a solution of the question is difficult to control, and as patients may be suffering from mixed infections, the question has been approached in a different manner by using the absorption method which Ehrlich introduced for the purpose of showing the specificity of amboceptors, etc., in immune sera.

The first study on the subject of specificity of opsonins was that of Bulloch and Western (1); they used normal serum and stated that there was a high degree of specificity of the opsonins as shown by their experiments with staphylococcus, B. pyocyaneus and B. tuberculosis.

They were able to show that after saturation of normal blood with staphylococcus, nearly all of the opsonin for that organism had been absorbed, while the opsonins for B. pyocyaneus and B. tuberculosis were largely retained.

This work, so far as I know, has not been confirmed. Simon (2) comes to quite opposite conclusions and states that there is no indication of the specificity of opsonins. He uses quite a different method from Wright in obtaining his index of opsonic power. Wright obtains his phagocytic index by averaging the number of organisms in a certain number (20 to 40) of leucocytes, while Simon neglects the average number of organisms per leucocyte and states as his result the percentage of leucocytes which phagocyte. He has made parallel tests with these methods and states that they give approximately the same results (5). It should be noted that he used B. typhosus, B. coli and staphylococcus in his absorption experiments, whereas Bullock and Western used B. tuberculosis, B. pyocyaneus and staphylococcus.

Potter, Ditman and Bradley (3) repeated Bulloch's experiments, using B. coli and staphylococcus, and they also failed to confirm the findings of Bulloch and Western. They found that saturation of normal serum with staphylococcus removed not only the opsonin for that organism, but also removed the opsonin for B. coli and vice versa.

In my experiments with normal human and normal rabbit serum, and these experiments have been repeated many times, I have uniformly found that saturation with staphylococcus removed not only its own opsonin, but also that for B. coli.

Normal rabbit serum was saturated at 37° C. for 30 minutes with staphylococcus aureus, and the mixture was then filtered

to remove the bacteria. The phagocytic index was obtained with a sample of the serum before and after saturation.

NORMAL RABBIT SERUM.

	Phagocytic Index.	
	Before saturation with Staphylococcus.	After saturation with Staphylococcus.
Staphylococcus	1.76	0.13
B. coli	0.94	0.15

This experiment was reversed by saturating with B. coli instead of with staphylococcus.

NORMAL RABBIT SERUM.

	Phagocytic Index.	
	Before saturation with B. coli, 1¼ hrs. at 37° C.	After saturation with B. coli.
B. coli	13.66	...
Staphylococcus	3.38	0.30

Here it is seen that saturation with B. coli removed nearly all the opsonin for staphylococcus, and that saturation with staphylococcus removes the opsonin for B. coli.

These results were uniformly true whatever the length of time during which the saturation was carried out (the duration of saturation was varied from 30 minutes to over 13 hours) and regardless of whether the saturating process was carried out at 0° or 37° C.

As these results were quite the opposite to those obtained by Bulloch and Western, and also at variance with the theory of the specificity of the opsonins which Wright everywhere assumes, and which the clinical side of opsonic work seems to justify, I made a further series of experiments using the same organisms that were used by Bulloch and Western in one of their tests, and while my results varied slightly at different times and witih different sera, the results may be looked upon as confirmatory of those of Bulloch and Western in that saturation with staphylococcus did not remove the opsonin for B. pyocyaneus to any extent.

NORMAL HUMAN SERUM.

	Phagocytic Index.	
	Before saturation over night at 37° C. with Staphylococcus.	After saturation.
Staphylococcus	2.80	0.46
B. pyocyaneus	10.26	8.13

This of itself seems to indicate that Bulloch and Western were right in asserting the existence of a high degree of specificity of opsonins. The reversal of the experiment, however, did not give the same results. Normal rabbit serum was saturated with B. pyocyaneus at 37° C. for two hours. The mixture was then filtered. The filtrate was tested and at the same time a test was made of the unsaturated serum, and it was found that B. pyocyaneus had reduced the phagocytic index for staphylococcus from 3.7 to 0.7. It seemed possible from this that B. pyocyaneus might be an exception to the general rule, so the following experiment was done.

Rabbit serum immune to guinea-pig corpuscles was divided into two portions, one of which was heated to 56° C. for 30 minutes. A portion of the heated serum and one of the unheated serum were then saturated with guinea-pig corpuscles and the phagocytic index to staphylococcus, streptococcus and B. pyocyaneus obtained.

RABBIT SERUM IMMUNE TO GUINEA-PIG BLOOD.

	Phagocytic Index.			
	Unheated.		Heated.	
	Before saturation with guinea-pig corpuscles.	After.	Before saturation.	After.
Staphylococcus	1.06	0.19	0.00	0.00
Streptococcus	2.48	0.46	0.14	0.03
B. pyocyaneus	7.06	2.71	3.75	3.02

This I think shows that B. pyocyaneus, at least the strain which I have used, is an exceptional organism in its behavior to opsonins, in that heating the serum does not destroy its opsonic power for this organism.

A further experiment was made to find out whether B. pyocyaneus has any other peculiarities.

NORMAL HUMAN SERUM BEFORE AND AFTER SATURATION AT 37° C. WITH STAPHYLOCOCCUS AUREUS FOR ONE AND ONE-HALF HOURS.

	Phagocytic Index.				
	Dilution 1 in 2.		Dilution 1 in 4.		
	Before saturation.	After saturation.	Before saturation.	After saturation.	Control containing no serum.
B. pyocyaneus	15.83	7.82	5.76	3.60	3.64
B. typhosus	3.81	0.15	1.60	0.14	0.23
B. coli	3.43	0.10	0.30	0.00	0.00
Staphylococcus aureus	2.48	0.52	0.81	0.38	0.64
Staphylococcus albus	4.66	1.00	1.56	0.70	0.00

This experiment shows that B. pyocyaneus is phagocyted spontaneously to a much greater extent than any of the other organisms tested, but that phagocytosis takes place better when serum is added; and it shows that the stronger the serum the more marked is the phagocytosis. In addition, it shows that the opsonin of normal serum for the entire list of organisms, including B. pyocyaneus, can be reduced or removed by saturation with staphylococcus aureus.

Bulloch's experiment with B. pyocyaneus was as follows: He saturated normal serum with staphylococcus, precipitated the cocci in the centrifuge, giving a supernatant fluid "A." A portion of this was then saturated with B. pyocyaneus, again placed in the centrifuge and a supernatant fluid "B" obtained.

	Phagocytic index.	
	Staphylococcus	B. pyocyaneus.
Normal human serum 1: 2.....	22.9	4.7
Normal human serum 1: 4.....		3.0
Normal human serum 1:2. After saturation with staphylococcus. Fluid A	0.5	4.0
Fluid A after saturation with B. pyocyaneus = Fluid B.....		0.4

The experiment was not reversed or results such as I have found might have been obtained. Such a result as in the first experiment is perfectly possible when B. pyocyaneus is used, for it undergoes spontaneous phagocytosis to a considerable extent, though the phagocytic index of normal serum for this organism is somewhat reduced by saturation with it. We can offer no explanation for the result obtained by Bulloch in the second experiment with Fluid B.

As to the specificity of the opsonins in normal serum for tuberculosis, I have not as yet been able to make any experiments.

Muir and Martin (4) have obtained results analogous to ours in that they were able to remove the opsonins for staphylococcus from normal serum by saturation with a combination of antigen and the corresponding amboceptors, as precipitins or lysins. They find that in their behavior under these circumstances the opsonins resemble complement.

Thus, it is seen that the results of Simon, Potter, Ditman and Bradley, Muir, and Martin, and my own all speak decisively against the specificity of the opsonins of normal sera, and I believe I have found a possible explanation for the opposite results of Bulloch and Western in their pyocyaneus experiment in the fact that B. pyocyaneus is readily susceptible to spontaneous phagocytosis.

During the course of these experiments it was thought possible that in the opsonic reaction complement or a non-specific complement-like substance might be necessary to activate the haptophoric groups which might be specific, and that therefore the apparent non-specificity of opsonins might be due to an insufficient amount of this complement or similar body, so that saturation with any variety of bacteria would remove all of this complement, leaving the haptophoric group for other bacteria, however, intact. A series of saturations at 0° C. were therefore carried out, but with quite negative results, in that the opsonins for both organisms were removed as in the saturations at 37° C. The bacteria were removed by filtering at 0° C. From these experiments at low temperature, it seems probable that the complement takes no part in opsonization.

Two experiments were done with immune sera—one a rabbit immunized to guinea-pig corpuscles, and the other a rabbit immunized to B. typhosus. The results of the first are given in the following table:

Rabbit Serum Immune to Guinea-Pig Corpuscles.

Dilutions.	Phagocytic Index to Guinea-pig Corpuscles.		
	Before saturation.	After saturation with guinea-pig corpuscles.	After saturation with streptococcus.
1-4	+	trace	+
1-8	+	—	+
1-16	—	—	—
1-32	—	—	—

Dilutions.	Phagocytic Index to Streptococcus.		
	Before saturation.	After saturation with guinea-pig corpuscles.	After saturation with streptococcus.
1-4	13.80	2.50	2.0
1-8	3.3	0.8	1.0
1-16	1.0	0.8	0.3
1-32	1.6	0.4	0.6

As the average number of erythrocytes ingested by the leucocytes is difficult to determine accurately, the method of dilution was used in the same manner as in agglutination tests. It will be observed that the phagocytosis of erythrocytes in the unsaturated serum disappeared when a dilution of 1 in 16 was reached; saturation of this serum with the antigen reduced the phagocytosis in a dilution of 1 in 4 to a mere trace, while on the other hand, saturation of this serum with streptococcus did not effect the immune opsonin for the antigen. This is evidence that the opsonin of this immune serum was specific. The second part of the table shows the behavior of the opsonins for a non-antigen—streptococcus. It is quite clear that there is here no question of specificity of the normal or non-immune opsonin, as practically as much opsonin for streptococcus is removed by saturation with guinea-pig corpuscles as by saturation with streptococcus itself.

The serum from a control rabbit showed entire absence of opsonin for guinea-pig erythrocytes.

A rabbit serum immune to B. typhosus contained sufficient opsonin to cause phagocytosis of typhoid bacilli, when tested in one of Wright's pipettes, in dilutions up to 1 in 1000, while phagocytosis with normal rabbit serum ceased in dilutions of 1 in 8 to 1 in 16. This serum was saturated with guinea-pig erythrocytes in the usual way, without any effect whatever on the immune opsonin for its antigen—B. typhosus.

A number of comparative observations by Dr. Meakins of the opsonic indices for several organisms following the injection of a vaccine of one of them for clinical purposes, apparently shows that the opsonin for the antigen is much more increased than that for the other organism. This was well demonstrated in sera following injection of meningo-coccus vaccine, which caused a greater rise in the opsonic curves than did any other vaccine which has been employed in the laboratory. Such sera did not show corresponding increase of opsonins for Staphylococcus aureus or Staphylococcus albus. We feel, however, that, owing to the errors inherent in the method, absolute conclusions cannot be drawn from such charts.

Conclusions.

(1) Following injections of bacterial vaccines, the increase of opsonins is probably due to the formation of immune opsonins which react specifically.

(2) In saturation experiments with normal sera we are dealing with normal or common opsonins, and these are not specific, since they can be removed by saturation with any one of a considerable number of bodies.

(3) In saturation experiments with immune sera we have both the immune and the common opsonin present; the former is quite specific, while the latter is not.

(4) B. pyocyaneus is quite susceptible to spontaneous phagocytosis.

We would further state that our conclusions are based on experiments which have been repeated a number of times, and that the results were so conclusive as to convince us that they do not merely represent differences due to the errors inherent in the Wright method.

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THE METHOD OF "FIXATION OF COMPLEMENT" IN THE DIAGNOSIS OF MENINGOCOCCUS AND GONOCOCCUS INFECTIONS.

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The phenomenon of "fixation of complement" has been well known since Bordet and Gengou (1) demonstrated that complement, added to a mixture of inactivated bacteriolytic serum and bacteria would not produce hæmolysis when sensitized erythrocytes were subsequently introduced. But it remained for Neisser and Sachs (2) to first make a practical application of this principle. They employed it in order to recognize human blood in medico-legal investigations. The method used by them may here be described briefly. A mixture of erythrocytes with the inactivated serum of an animal immunized to them, is spoken of as a hæmolytic system. When to such a system fresh complement is added, hæmolysis occurs. But if the complement should first be added to a mixture of the inactivated serum of an animal immunized to human serum, plus a trace of human serum, and then subsequently be added to the above hæmolytic system, no hæmolysis occurs. That the trace of human serum is necessary for this phenomenon to occur may be demonstrated by omitting it, and then hæmolysis will proceed as before. Neisser and Sachs explained this phenomenon by supposing that the human serum contains receptors, and that the inactivated serum immune to human serum contains amboceptors which bind the complement to the receptors, and thus prevent its action in the hæmolytic system. They also found that the smallest trace of human serum, at times even 0.000,001 cc., was sufficient to produce this phenomenon. Then Wassermann and Brück (3) applied this principle, not to detect the presence of specific serum albumins, but to detect the presence or absence of small amounts of dissolved bacterial products (antigens) or their corresponding anti-bodies in serum or inflammatory exudates. The first disease studied by them was typhoid. When an extract of typhoid bacilli (dissolved bacterial substances), typhoid patient's serum and complement were mixed and incubated for a short time, it was found that the complement would not reactivate a hæmolytic serum. Thus it was concluded that the patient's serum contained amboceptors for the dissolved bacterial substances. They also demonstrated the presence of bacterial substances in the serum. If to the serum of a typhoid patient, the inactivated serum of an animal highly immunized to typhoid bacilli, and fresh complement be added, it is found that hæmolytic serum is again not reactivated by the complement contained in the mixture. In other words, the complement has been bound. We may therefore conclude that the patient's serum contains dissolved bacterial substances (bacterial receptors) or antigens. These writers then applied this method to the study of tuberculosis and the tuberculin reaction (4). Their first step was to demonstrate the presence of antituberculin in tuberculous organs. But in the blood of untreated patients no anti-tuberculin could be demonstrated. Following the administration of tuberculin, however, antituberculin could be detected in the blood. It is very unfortunate from a diagnostic standpoint that tuberculin or antituberculin is not present in the blood of untreated patients with localized tuberculosis. Brück (5), however, has made a very interesting observation on the blood of a patient suffering from general miliary tuberculosis. He found that in the early stages of the disease tuberculin was present; but during the course of the disease this disappeared and antituberculin could be demonstrated. Before the lethal termination, however, the tuberculin was again detected. Here we have a method of diagnosis for the early stages of miliary tuberculosis, a disease which is notoriously uncertain in its early manifestations.

About the same time Wassermann, Neisser, and Brück (5) investigated the possibilities of this method for the diagnosis of syphilis. The syphilitic origin of general paresis and locomotor ataxia was likewise investigated by studying the cerebro-spinal fluid of suspected patients. The antigens were obtained from the organs of a syphilitic fœtus (see below) and the anti-bodies (amboceptors) from the inactivated serum of an immunized ape.

Besides the above writers, Wassermann and Plaut (7) Neisser, Brück and Schught (8), Bab (9), Schütze (10), Marie and Levaditi (11), Morgenroth and Stertz (19), and P. Mühlens (12), have reported similar investigations concerning syphilis. Müller and Oppenheim (13) have studied one case of gonococcus infection, and Brück (14), two cases of meningococcus and one case of streptococcus infection. Neufeld and Hüne (15) have made application of the method in typhoid and para-typhoid fever and hog cholera, and Neisser and Sachs (16) and Schütze (17) have further reported on its use in forensic medicine.

Technique.

As previously stated, the object of the test is to detect the presence or absence in the serum investigated of (a) the antigen, the infecting organism or cell, or (b) the anti-body (amboceptor) for the same organism or cell, either or both of which may be present in the serum.

The patient's serum, which is to be tested, is collected in the usual way, and the complement containing serum is obtained from the blood of a normal animal. Then the antigen or anti-body with which the patient's serum is to be mixed is procured in the following manner:

(a) In the first instance an emulsion of the suspected in-

fecting organism is made in 0.85% NaCl solution. The age of the growth is immaterial; but where a pure culture of the organism is not obtainable, as in syphilis, another measure is necessary. In this case (6) a syphilitic fœtus is obtained and the organs (liver, spleen, kidneys, supra-renal glands, heart, and lungs) are macerated in 0.85% NaCl solution, and placed in a cold chamber for 24 hours. At the end of this time this emulsion is filtered until the filtrate is clear. It is considered that this fluid contains the syphilitic antigen in solution. But there is one objection to this method, and that is that this antigen action is lost after six days. A much better method (11) is to put the fœtal organs in a desiccator and dry them thoroughly, when a powder may be obtained containing the syphilitic antigen, which retains its power for months. When the experiment is to be performed a small quantity of this powder is thoroughly mixed with 0.85% NaCl solution and then filtered, and the filtrate will then contain the syphilitic antigens ready for immediate use. A third method is to keep the organs in a frozen condition until required (19).

(b) The anti-bodies of the infecting organism are obtained by immunizing an animal to the special organism. Then the serum of this animal is collected in the usual manner and inactivated at 56° C. This serum should then contain the amboceptors for the immunizing organism, but no complement.

Finally the hæmolytic system should be prepared. This consists of sensitized erythrocytes, prepared by mixing together equal volumes of erythrocytes (5 per cent emulsion), and inactivated hæmolytic serum. The strength of the latter should be tested and enough added to the red cells to cause hæmolysis when complement is introduced.

These substances having all been prepared, the experiments may now be undertaken. The first step is to demonstrate the presence or absence of specific anti-bodies. This is undertaken in the following manner:

The patient's inactivated serum is diluted to varying strengths and a known quantity (0.5 cc.) is placed in each of a series of small test tubes. Then to each of these is added an equal volume of bacterial emulsion and also the same volume of normal serum containing complement (1-10), and the total placed in the incubator for half an hour. The sensitized corpuscles are now added to each tube and the mixture incubated for two hours (see Table I below). They are then placed in the ice chest over night. The tubes are finally

Table I.

Patient's serum inactivated at 56° C.	Bacterial emulsion.	Normal rabbit serum 1-10.	Rabbit serum immune to erythrocytes inactivated at 56° C. 1-10.	Emulsion of erythrocytes 5%.
0.5 cc. 1-10	0.5 cc.	0.5 cc.	0.5 cc.	0.5 cc.
0.5 cc. 1-20	0.5 cc.	0.5 cc.	0.5 cc.	0.5 cc.
Etc.	Etc.	Etc.	Etc.	Etc.

examined to determine the presence or absence of hæmolysis. If the former has occurred, we know that the complement was not fixed to the bacterial receptors. Therefore, no anti-bodies were present in the patient's serum. But on the other hand, if hæmolysis is not present, we infer that the complement was bound to the bacterial receptors by the anti-bodies contained in the patient's serum, or, in other words, "fixation of the complement" or "Komplementbindung" has occurred. This is regarded as then constituting a specific reaction.

If "fixation of the complement" has not been demonstrated, it is necessary to proceed with the second experiment, or that for the detection of the antigen. The method for this procedure is practically the same as the former. The only difference is the substitution of an inactivated bacteriolytic serum for the bacterial emulsion. (See Table II.) As

Table II.

Patient's serum inactivated at 56° C.	Animal serum immunized to special bacteria. Inactivated at 56° C. 1-10.	Normal rabbit serum.	Rabbit serum immunized to erythrocytes. Inactivated at 56° C. 1-10.	Emulsion of erythrocytes 5%.
0.5 cc. 1-10	0.5 cc.	0.5 cc.	0.5 cc.	0.5 cc.
0.5 cc. 1-20	0.5 cc.	0.5 cc.	0.5 cc.	0.5 cc.
Etc.	Etc.	Etc.	Etc.	Etc.

in the former experiment, hæmolysis or no hæmolysis will indicate a negative or a positive result. No hæmolysis signifies that the complement has been "fixed"; that is to say that it has become attached to the antigen in the patient's serum, through the medium of the immune bodies in the immune animal's serum.

In explanation of this reaction, our knowledge at the present time enables us to say that besides bacterial amboceptors, other bodies in immune serum, such as precipitins (18) have also the power to bind complement. From the diagnostic standpoint, it is immaterial which of these bodies is active, all being the products of infection or immunization.

In order to place reliance upon such experiments, it is necessary that a control be made by substituting normal human serum for that of the patient.

In the following protocols the foregoing methods have been carried out and checked by the necessary control tests.

Cerebro-Spinal Fever.

Case I.—E. H. Hospital No. 58,109, male, aged 34.

The illness began on February 13, 1907, and from this time the ordinary features of cerebro-spinal fever developed. He was admitted to the hospital on February 16, 1907. On the following day lumbar puncture was performed, and 15 cc. of turbid fluid were withdrawn. Cover glasses and cultures showed the presence of Diplococcus intracellularis. He gradually grew worse and died on February 23.

On February 18, the patient's serum was tested for the presence of amboceptors for Diplococcus intracellularis, by the method of complement fixation. The following chart (III) shows the experiments in a graphic form.

Case II.—H. L. Hospital No. 57,780, male, white, aged 19.

The patient took ill on January 18, 1907. He was admitted to the hospital on January 19. Lumbar puncture was performed at once, and 12 cc. of fluid were removed. This was turbid and contained many pus cells with intra- and extra-cellular diplococci,

decolorizing when stained by the Gram method. Cultures proved the organisms to be Diplococcus intracellularis. The patient died on February 15.

The post-mortem examination revealed typical lesions of epidemic cerebro-spinal meningitis. On January 31 the patient's serum was tested for the presence of meningococcal anti-bodies. The result was positive, as is shown below in Chart III.

CASE III.—E. C. Hospital No. 56,460, female, aged 17.

Early on the morning of March 11, 1907, the patient had a severe rigor, with pain in the head and neck, nausea, and vomiting. These symptoms persisted to a marked degree, and she was admitted to the hospital on March 15.

CHART III. MENINGOCOCCUS MENINGITIS.

No.	Patient's serum inactivated at 56° C.	Meningococcus emulsion.	Normal rabbit's serum 1 in 10.	Rabbit's serum immune to guinea-pig corpuscles inactivated at 56° C. 1 in 10.	Guinea pig erythrocytes 5%.	Result.
1	.....	0.5 cc.	0.5 cc.	0.5 cc.	0.5 cc.	Hæmolysis complete.
2	.....	.....	"	"	"	"
3	.....	.....	.....	"	"	" absent.
	Normal serum.					
4	0.5 cc. 1 in 10	....	0.5 cc.	"	"	" complete.
5	" 1 " 10	0.5 cc.	"	"	"	"
6	" 1 " 20	"	"	"	"	" "
7	" 1 " 40	"	"	"	"	" "
8	" 1 " 80	"	"	"	"	" "
9	" 1 "160	"	"	"	"	" "
	Case I.					
10	0.5 cc. 1 in 10	.....	"	"	"	" "
11	" 1 " 10	0.5 cc.	"	"	"	" absent.
12	" 1 " 20	"	"	"	"	" "
13	" 1 " 40	"	"	"	"	" "
14	" 1 " 80	"	"	"	"	" "
15	" 1 "160	"	"	"	"	" partial.
	Case II.					
16	0.5 cc. 1 in 10	.....	"	"	"	" complete.
17	" 1 " 10	0.5 cc.	"	"	"	" absent.
18	" 1 " 20	"	"	"	"	" "
19	" 1 " 40	"	"	"	"	" "
20	" 1 " 80	"	"	"	"	" "
21	" 1 "160	"	"	"	"	" partial.
	Case III.					
22	0.5 cc. 1 in 10	.....	"	"	"	" complete.
23	" 1 " 10	0.5 cc.	"	"	"	" absent.
24	" 1 " 20	"	"	"	"	" "
25	" 1 " 40	"	"	"	"	" "
26	" 1 " 80	"	"	"	"	" partial.
27	" 1 "160	"	"	"	"	" complete.

On examination the patient was drowsy, eyes partly closed, no photophobia or strabismus. A suggestion of herpes was present at the right angle of the mouth. There were no subcutaneous or submucous hæmorrhages. Temperature was 103.8 degrees Fahrenheit. The knee-jerks were absent, there was no clonus and Babinski's sign was not obtained. There was marked stiffness of the neck and Kernig's sign was positive on both sides. The white blood corpuscles numbered 22,040. On March 16, a lumbar puncture was done and 40 cc. of slightly yellowish fluid were obtained under a pressure of 390 mm. (of fluid). Microscopical examination showed the fluid to contain many cells, both mononuclear and polymorphonuclear. Lumbar puncture was repeated on March 18, with a similar result. Smears and cultures did not show any organisms. Up to this time the patient had remained in the same condition as on entrance to the hospital, but now she gradually began to improve. Kernig's sign, stiffness of the neck and the headache disappeared, and the patient was discharged on April 17.

On March 19 the patient's serum was tested for anti-bodies to the meningococcus by "fixation of complement" with a positive result. (See Chart III.)

A few explanations may be made in regard to the controls, which are of great importance in correctly carrying out the experiments.

Tubes 1 and 2 show that when the patient's serum and the organism are omitted, fixation of complement does not take place. In 3 no hæmolysis has occurred, since the tube contained no complement. Tubes 4, 10, 16, and 22 are introduced to demonstrate the fact that the absence of bacteria will allow hæmolysis to proceed in spite of the presence of inactivated human serum. The tubes 5 to 9 inclusive show that normal inactivated human serum does not contain immune bodies for the organism tested, the complement remaining unfixed, and thus allowing hæmolysis to take place.

Considering now Cases I, II and III, in which "fixation of complement" has been demonstrated, it will be noted that positive results occur within certain varying degrees of dilution of the amboceptor containing sera, showing that the amount of complement fixing substance (amboceptor) may vary in different cases of any one disease. In these three cases it is apparent that the sera possess qualities different from those of normal serum. Plainly, the inference is, that the reaction denotes a present or recent infection with the meningococcus. Corroborative proof of this inference was in fact furnished by Cases I and II, whereby the meningococcus was obtained in culture from the fluid in the spinal canal. All results being negative in Case III, the clinical diagnosis of meningococcus meningitis was confirmed by the positive result obtained in this experiment of "fixation of complement."

CHART IV. GONORRHŒAL ARTHRITIS.

No.	Human serum inactivated at 56° C.	Gonococcus emulsion.	Normal rabbit serum 1 in 10.	Rabbit serum immune to guinea-pig corpuscles inactivated at 56° C. 1 in 10.	Guinea pig corpuscles 5%.	Result.
	Normal.					
1	....	1 cc.	0.5 cc.	0.5 cc.	0.5 cc.	Hæmolysis complete.
2	....	.....	"	"	"	" "
3	....	.....	.....	"	"	" absent.
4	1 cc. 1 in 10	.....	0.5 cc.	"	"	" complete.
5	" 1 " 10	1 cc.	"	"	"	" "
6	" 1 " 20	"	"	"	"	" "
7	" 1 " 40	"	"	"	"	" "
8	" 1 " 80	"	"	"	"	" "
9	" 1 "160	"	"	"	"	" "
	Case I.					
10	1 cc. 1 in 10	.....	"	"	"	" "
11	" 1 " 10	1 cc.	"	"	"	" absent.
12	" 1 " 20	"	"	"	"	" "
13	" 1 " 40	"	"	"	"	" "
14	" 1 " 80	"	"	"	"	" "
15	" 1 "160	"	"	"	"	" slight.
	Case II.					
16	1 cc. 1 in 10	.....	"	"	"	" complete.
17	" 1 " 10	1 cc.	"	"	"	" absent.
18	" 1 " 20	"	"	"	"	" "
19	" 1 " 40	"	"	"	"	" "
20	" 1 " 80	"	"	"	"	" "
21	" 1 "160	"	"	"	"	" complete.
	Case III.					
22	1 cc. 1 in 10	.....	"	"	"	" complete.
23	" 1 " 10	1 cc.	"	"	"	" complete.
24	" 1 " 20	"	"	"	"	" "
25	" 1 " 40	"	"	"	"	" "
26	" 1 " 80	"	"	"	"	" "
27	" 1 "160	"	"	"	"	" "

GONORRHEAL ARTHRITIS.

CASE I.—D. M. Medical No. 20,780, male, aged 32.

The patient contracted gonorrhœa in December, 1906, and this was followed on December 28 by an attack of acute polyarthritis. On March 21, 1907, his blood was tested for gonococcal

anti-bodies. At this time there was a chronic arthritis and also a chronic urethritis. (See Chart IV.)

Case II.—N. B. Hospital No. 57,936, male, aged 35.

The patient had had gonorrhœa six times. The last attack was in November, 1906. Early in December he developed an acute polyarthritis, involving chiefly the hips and the right ankle.

On March 21, 1907, when his blood was tested, physical examination showed a chronic arthritis, chronic urethritis, and chronic prostatitis. (See Chart IV.)

Case III.—C. B. Hospital No. 57,952, male, aged 35.

The patient had gonorrhœa in November, 1906, which was followed in January, 1907, by an acute polyarthritis. On March 21, the joint involvement was slight, but there was still a slight chronic urethritis.

On this date his blood was examined for anti-bodies by "fixation of complement." (See Chart IV.)

Chronic Gonorrhœal Urethritis and Prostatitis.

Case IV.—J. G. Dispensary No. E3107, male, aged 19.

The patient contracted his first attack of gonorrhœa three months before admission. A chronic urethral discharge continued, and on admission examination showed a chronic urethritis and a mild grade of prostatitis. The patient's blood was examined on April 3, 1907. (See Chart V below).

Case V.—J. S. Dispensary No. E133, male, aged 29.

The patient developed an acute attack of gonorrhœa in the middle of January, 1907. This was of a very severe character and persisted until admission, April 3. In February he had an acute cystitis and prostatitis. The cystitis subsided, but on admission there was still a chronic urethritis and prostatitis.

His blood was examined on April 3. (See Chart V below).

Chart V.

No.	Human serum inactivated at 56° C.	Gonococcus emulsion.	Normal rabbit serum 1 in 10.	Rabbit serum immune to guinea-pig corpuscles inactivated at 56° C. 1 in 10.	Guinea-pig corpuscles 5%.	Result.
	Normal.					
1	... .	0.5 cc.	0.5 cc.	0.5 cc.	0.5 cc.	Hæmolysis complete.
2	.....	.....	"	"	"	"
3	.....	.....	... . .	"	"	absent.
4	1 cc. 1 in 10	.....	0.5 cc.	"	"	complete.
5	" 1 " 10	0.5 cc.	"	"	"	"
6	" 1 " 20	"	"	"	"	"
7	" 1 " 40	"	"	"	"	"
8	" 1 " 80	"	"	"	"	"
9	" 1 "160	"	"	"	"	"
	Case IV.					
10	1 cc. 1 in 10	.....	"	"	"	"
11	" 1 " 10	0.5 cc.	"	"	"	absent.
12	" 1 " 20	"	"	"	"	"
13	" 1 " 40	"	"	"	"	"
14	" 1 " 80	"	"	"	"	partial.
15	" 1 "160	"	"	"	"	"
	Case V.					
16	1 cc. 1 in 10	.....	"	"	"	complete.
17	" 1 " 10	0.5 cc.	"	"	"	absent.
18	" 1 " 20	"	"	"	"	"
19	" 1 " 40	"	"	"	"	"
20	" 1 " 80	"	"	"	"	"
21	" 1 "160	"	"	"	"	partial.

The technique and the controls employed in this series of gonococcal infections were identical with those used for the cases of meningitis.

In Case I "fixation of complement" occurred when the patient's serum was diluted 1 in 80 or even 1 in 160; in Case II, 1 in 80; in Case III, 1 in 80; in Case IV, 1 in 40, and in Case V, 1 in 80.

Although the technique in these experiments is much more difficult than that in the precipitin reaction, and the results perhaps no more specific, yet the end reaction is much more definite. As Neisser and Sachs have shown "fixation of the complement" may be present in a much higher dilution of the patient's serum than that which would give a visible precipitate. It might here be urged that the difficulties of technique in this method of diagnosis almost prohibit the method for routine work. Yet in the investigation of special cases, or in the study of the etiology of certain affections, this method offers great possibilities.

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"DIVERSION OF COMPLEMENT" IN HÆMOLYSIS.

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The discovery by Pfeiffer (1) in 1895 that large amounts of immune serum did not protect an animal from the cholera vibrio, although smaller amounts were efficacious, called attention to the relationship between the components of bactericidal immune serum. During the next few years Loeffler and Abel (2), Leclainche and Morel (3) made similar observations in working with other organisms. But it was not until 1901 that an explanation of this phenomenon was sought experimentally. In this year Neisser and Wechsberg (4) demonstrated an analogous reaction in vitro and proceeded to seek the explanation. They studied the effect of a bacteriolytic immune serum when varying amounts of the inactivated serum were employed. The quantity ranged from .0005 cc. to 1 cc. To each of these amounts constant volumes of normal serum and bacterial emulsion were added. They found no bacteriolysis where large and small amounts of immune serum were used. But where medium amounts were employed, the bacteriolysis was complete.

In a second series, the amounts of the reactivating serum were varied, while the inactivated immune serum and the bacterial emulsion remained constant. The result was as in the first instance; that is, with relatively small amounts of reactivating normal serum, bacteriolysis did not occur. By further experiments, they demonstrated that inactivated normal serum was inert, and also that normal serum having slight bacteriolytic action was rendered inactive by the addition of a large quantity of inactivated immune serum. Furthermore they showed that agglutinins did not play a part in this phenomenon. Similar results were obtained when these experiments were repeated, using hæmolytic serum and erythrocytes.

From these experiments Neisser and Wechsberg conclude that where the amboceptors are in great excess, a portion combine with the complement, leaving some free, and that these free amboceptors unite with the receptors before the activated amboceptors do, and thus the complement-amboceptor group is rendered inert.

Gay (5), however, in 1905, performed experiments which seemed to contradict the above conclusions. He held that it is the precipitation (produced by the union of serum and antiserum) which causes the diversion of complement. In the experiments performed by Gay, rabbit serum immune to ox corpuscles was used. The red cells were washed very thoroughly, which he claims was not done in the Neisser-Wechsberg experiments, in order to exclude the possibility of any ox serum being present. He first produced varying degrees of precipitation by adding constant amounts of ox serum to varying amounts of inactivated immune rabbit serum. To these mixtures and to controls, in which no ox serum was present, equal amounts of normal rabbit serum and sensitized ox corpuscles were added. Hæmolysis occurred in inverse ratio to the amount of precipitate found. Where there was a marked precipitate, no hæmolysis occurred; while in those tubes in which there was no precipitate, and in the controls, hæmolysis was complete.

Thus it will be seen that the views of Neisser and Wechsberg and those of Gay are directly opposed, and both are supported by careful experimentation. It was with the object of approaching this problem from a somewhat different standpoint that the following experiments were undertaken.

A rabbit was highly immunized to guinea-pig corpuscles. The immune serum diluted 1 in 2400 caused complete hæmolysis. In order to overcome possible sources of error, the erythrocytes used were washed in 0.85 per cent sodium chloride solution *twelve* times, 15 cc. of the salt solution being used for each washing. Thus any serum attached to the corpuscles would be reduced to an infinitesimal quantity. In the collection of the immune and normal sera, the greatest care was exercised to prevent hæmolysis or contamination with any foreign material. In addition, when the substances were combined, unnecessary agitation was carefully avoided. In fact, every source of error was eliminated as carefully as possible.

Experiment I.

The rabbit serum immune to guinea-pig corpuscles was heated to 56° C. for half an hour. It was then diluted ten times, and 1.5 cc. of this dilution was added to 0.1 cc. of normal rabbit serum, which had been diluted 100 times. This mixture was incubated at 37° C. for half an hour to allow combination, and then 1.5 cc. of 5 per cent guinea-pig corpuscles in 0.85 per cent sodium chloride solution were added. The total was incubated for one hour at 37° C. At the end of this time the corpuscles were carefully precipitated by centrifugalization and the degree of hæmolysis noted. None was present.

The supernatant fluid was carefully pipetted off, and to this 0.2 cc. of normal rabbit serum (1 in 100) was added, and this mixture again incubated for half an hour. Then 1.5 cc. of guinea-pig corpuscles were added and the total incubated for one hour as before. The corpuscles were again centrifugalized and the degree of hæmolysis observed. Still there was none present.

The supernatant fluid was again treated as in the first instance, except that now 0.4 cc. of normal rabbit serum (1 in 100) was introduced. It was found there was still no hæmolysis. The procedure was repeated, employing a larger amount, 1.5 cc., of normal rabbit serum (1 in 100). When this part of the experiment was completed, it was found that total hæmolysis had occurred. This experiment was controlled in the following way. Equal quantities of inactivated

rabbit's serum immune to guinea-pig corpuscles (1 in 10) and 5 per cent emulsion of guinea-pig erythrocytes were mixed and no hæmolysis occurred; but when normal rabbit serum (1 in 5) was added in equal volume, the hæmolysis was complete. These results are shown in the following chart.

CHART I.

	Rabbit's serum immune to guinea-pig corpuscles inactivated at 56° C. 1-10.	Normal rabbit serum. 1 100.	Guinea-pig corpuscles 5%.	Time of incubation.	Result.
A	= 1.5 cc.	0.1 cc.		½ hour.	
A_1	= A.		1.5 cc.	1 "	No hæmolysis.
B	= Supernatant Fluid of A_1	0.2 cc.		½ "	
B_1	= B.		1.5 cc.	1 "	" "
C	= S. F. of B_1.	0.4 cc.		½ "	
C_1	= C.		1.5 cc.	1 "	" "
D	= S. F. of C_1.	1.5 cc.		½ "	
D_1	= D.		1.5 cc.	1 "	Complete hæmolysis.

Controls.

	Rabbit's serum immune to guinea-pig corpuscles, inactivated at 56° C. 1-10.	Normal rabbit serum. 1-5.			
I	1.5 cc.		1.5 cc.	1 "	No hæmolysis.
II	1.5 cc.	1.5 cc.	1.5 cc.	1 "	Complete "

EXPERIMENT II.

The corpuscles used in the three parts of the first experiment in which no hæmolysis occurred were carefully preserved. These were now repeatedly washed in 0.85 per cent sodium chloride solution until all the serum was removed. Undue shaking or any other cause of artificial hæmolysis was carefully avoided.

These corpuscles were now treated with 1.5 cc. of normal rabbit serum (1-5) and incubated for one hour. Complete hæmolysis occurred. But on the other hand the mixture of ordinary guinea-pig corpuscles (5 per cent emulsion) and normal rabbit serum (1-5), in the same amounts as before, produced no laking whatsoever. This is shown in the following chart.

CHART II.

	Corpuscles.	Normal rabbit's serum (1-5).	Time of Incubation.	Result.
I	From A_1, B_1 and C_1 of Experiment I..... 1.5 cc.	1.5 cc.	1 hour.	Complete hæmolysis.
II	Unused corpuscles as in Experiment I... 1.5 cc.	1.5 cc.	1 "	No hæmolysis.

EXPERIMENT III.

Inactivated rabbit serum immune to guinea-pig corpuscles (1-10) in the amount of 1.5 cc. was combined with 2.2 cc. of normal rabbit serum (1 to 100) and incubated for half an hour at 37° C. This amount of normal rabbit serum was exactly the same as the total amount used in the four parts of the first experiment. At the end of this time 1.5 cc. of guinea-pig corpuscles were added and all incubated for one hour. They then were centrifugalized as in the other experiments, and it was found that no hæmolysis had occurred. This is shown in Chart III.

CHART III.

	Rabbit's serum immune to guinea-pig corpuscles inactivated at 56° C. 1-10.	Normal rabbit serum 1-100.	Guinea-pig corpuscles 5%.	Result.
A	1.5 cc.	2.2 cc.		
A_1	= A.		1.5 cc.	No hæmolysis.
	Control.			
	1.5 cc.		1.5 cc.	" "
		2.2 cc.	1.5 cc.	" "

It will be seen from these experiments that a certain definite relationship must be reached between the amount of amboceptors and complement before hæmolysis will take place. From the first experiment, it is apparent that after the primary incubation, both activated and inactivated amboceptors are present in each of the first three parts. The inactivated amboceptors, however, seem to have the greater affinity for the receptors and, being greatly in excess, were immediately bound. This process occurred successively, until all or nearly all of the amboceptors were removed or activated. That this was brought about in two ways is made probable; first by the removal of inactivated amboceptors attached to the blood cells, and second, by the gradual addition of the complement.

The proof that the first of these events occurred is demonstrated in the second experiment, in which hæmolysis of the sensitized corpuscles occurred by the simple addition of sufficient complement. That the relatively great preponderance of amboceptors over the complement was the cause of the absence of hæmolysis is the most probable inference when the result of the third experiment is considered. In this case, as is shown, the first stage of Experiment I was repeated with the exception of one detail. The amount of complement used is equal to the total amount added in all stages of the first experiment. Yet there was no hæmolysis, while the same amount of complement had previously given a positive result. But the cause of the difference is very apparent. In the third experiment, there was a diversion of complement after the manner stated above. In the first experiment there was also diversion in the previous stages, until, by the successive removal of amboceptors by the corpuscles and the fractional addition of the complement, the relation between the complement and the amboceptors had reached the proper proportion. Then hæmolysis occurred.

That a precipitate formed by the mixture of immune serum with an homologous normal serum may cause "*fixation*" of complement has been well demonstrated by Gay, (5) Muir and Martin (6), Moreschi and others. Muir and Martin found that a visible precipitate was unnecessary for this to occur, and that even 0.00001 cc. of homologous serum would give complete "fixation." In the above experiments the great care taken to remove the guinea-pig serum from the corpuscles reduces the possible amount of serum to .0000000000001 cc.

at the most. In view of these facts, the chance of such a reaction being accountable for the phenomena observed may be disregarded.

Conclusions.

I. Receptors may have a greater affinity for inactivated than for activated amboceptors.

II. Receptors may remove amboceptors in the presence of complement without hæmolysis taking place.

III. The precipitate due to the reaction of precipitin and precipitinogen is not necessary for "diversion" of the complement.

IV. "Diversion of complement" occurs when the amboceptors are greatly in excess of the complement, and hæmolysis occurs when these substances are present in proper proportions.

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NOTE ON THE PRODUCTION OF AN AGGLUTINATING SERUM FOR BLOOD PLATELETS.

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In precipitating blood corpuscles contained in a blood-sodium citrate or blood-sodium oxalate mixture, it is found that the supernatant fluid is always opaque, while the supernatant fluid obtained after rewashing such precipitated corpuscles in sodium chloride solution is clear and transparent. To investigate the cause of this opacity, the opaque supernatant fluid was removed and again centrifugalized at a high speed for one hour. The fluid now became almost clear and a white sediment was found, which on microscopical examination was seen to consist entirely of blood platelets. By mixing this thoroughly in salt solution, a homogeneous emulsion of the platelets may be obtained.

Having obtained such an emulsion of blood platelets, free from red blood cells, it was next attempted to produce a serum containing immune bodies to these platelets. For this purpose the platelets obtained from 5 to 10 cc. of human blood were injected into the ear vein of a rabbit. Several such injections were made and the agglutinating power of the serum was tested. As it was difficult to obtain large amounts of the platelet emulsion, the tests were made by the microscopical method employed in performing the Widal test. It was found that such a serum had acquired the power of causing marked agglutination in the emulsion of platelets. Where strong emulsions are employed, the reaction is easily seen by the naked eye. In low dilutions such a serum also causes the clumps of platelets to disintegrate after a short time. It has lytic as well as agglutinating properties for platelets.

The following protocol shows the result of such an experiment, and also the fact that such a serum has no action on the platelets of an animal of the same species.

Rabbit A.

July 3. Platelets obtained from 10 cc. normal human blood injected into the marginal ear vein of a rabbit.

July 9. Injection as above.

July 19. Injection as above.

July 25. Serum tested as to agglutinating power for platelets.

	Dilution.		Results.
Rabbit immune serum.	1:10	Emulsion human platelets.	Instantaneous agglutination. Lysis after 1 hour.
Do.	1:50	Do.	Agglutination well marked.
Do.	1:100	Do.	Agglutination definite in 1 hour.
Do.	1:200	Do.	Agglutination doubtful.
Do.	1:1	Emulsion rabbit platelets.	No reaction.

It next seemed important to determine whether such a serum exhibits hæmagglutinating and hæmolytic powers, as well as agglutinating and lytic powers for platelets. The hæmagglutinating and hæmolytic powers of the serum of a normal rabbit for human red blood corpuscles was therefore tested, and it was found that it caused hæmolysis in dilution of 1:1 and slight agglutination in dilution of 1:10, but in greater dilutions was inactive. It caused absolutely no agglutination of human platelets, even when undiluted. This rabbit was then inoculated with platelets from 10 cc. of blood, and one week later its agglutinating and lytic powers were tested. It now caused marked agglutination of human platelets in dilutions of 1:20. The hæmolytic and hæmagglutinating powers were not changed.

It should be stated, however, that several more active agglutinating sera for platelets were found to have slightly more action on red blood corpuscles than has the untreated

normal rabbit serum. It is very difficult to obtain emulsions of platelets for injection, however, which do not contain an occasional red blood corpuscle. From what we know of other cytolytic sera, it is not improbable that such sera, if very active, even if produced by the injection of pure platelets, may have some action on red blood corpuscles. The above experiment, however, which was repeated several times speaks for a considerable grade of specific action.

To approach this problem in another way, we produced a hæmolytic serum by the injection into rabbits of human red blood corpuscles obtained by defibrination. The platelets are always caught in the fibrinous meshwork, and it is probable that such corpuscles have mixed with them few or no platelets. By the injection of these corpuscles into a rabbit, a serum having hæmolytic action in dilution of 1:600 was obtained. The agglutinating power for human platelets was now tested, and it was found that such a serum was entirely inactive, even in dilution of 1:1.

These experiments seem to speak quite definitely against a genetic relationship between platelets and red blood corpuscles. This question seems to have been quite definitely settled by the observations of Wright[1] on the origin of blood platelets. These experiments, however, offer additional evidence against the view of Kemp and others that platelets are derived from red blood corpuscles.

The method of obtaining platelets and the production of immune sera also obviously offers an opportunity for the study of the rôle of blood platelets in coagulation. In order to study this question satisfactorily, however, large amounts of the active sera are necessary. Preliminary experiments made by mixing such active serum with human blood and testing the variation in coagulation time so caused by means of Boggs' modification of the Brodie-Russell coagulometer have given negative results.

[1] Virchow's Archiv.

SOME OBSERVATIONS UPON BLOOD PRESSURE AND PULSE FORM.

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The Strasburger Method for the Determination of Minimal Blood Pressure—Its Inaccuracies, Their Correction, and Its Actual Value.

The value of the clinical determination of the minimal as well as of the maximal blood pressures has been so clearly demonstrated by the work of Erlanger and Hooker (1), and the later writers, Janeway (2), v. Recklinghausen (3), Sahli (4), Strasburger (5), Fellner (6), and D. Gerhardt (7), that the question of the method by which these determinations will be made becomes all important. By far the most accurate, most certain, and easiest of execution in the hospital or laboratory is the original method of Erlanger (8), made with his elaborate and rather bulky apparatus, which is otherwise almost perfect in point of manipulation. The disadvantages are (*a*) bulk and weight, and (*b*) expense, which have thus far been sufficient to keep it out of the hands of many practitioners and have prevented it from coming into use in making the routine blood pressure estimations in the wards of even the best hospitals. The bulk of the apparatus has also prevented its use in the house to house visits of practicing physicians.

The second method of determining minimal pressure, that of T. C. Janeway, consists in watching the movement of the mercury-column as the pressure in the cuff of the Riva-Rocci apparatus is lowered and in determining the point at which the oscillations due to the pulse are maximal. This method is successful mainly with pulses of large volume.

The third method, that of Sahli and Masing, consists in taking the pulse tracing at the wrist while compressing the arm above with the Riva-Rocci apparatus; pulse tracings are taken at different levels of pressure, and the points below which no further increase in the size of the pulse wave takes place are determined. In the cases in which I have controlled this method with the Erlanger apparatus, the results have been quite accurate, provided the slightest slipping of the sphygmograph was prevented or was corrected by careful readjustment; the process involves, however, a large amount of time and care, and limits the application of the method to the quietest of patients.

A fourth form of apparatus is the hæmodynamometer of Oliver, in which the movement of a bubble of stained alcohol in a closed-tube manometer is watched and the maximum of its movement selected; the error of the method is due to the varying value of 1 mm. of movement in different parts of the pressure scale.

The fallacy of the observation by Oliver's method is obviated in the sphygmoscope of Pal (9), in which the pressure on both sides of the column of alcohol is the same, except for the slight change of pressure due to the pulse wave. The Pal apparatus in its present form is, however, at least as bulky and as costly as the Erlanger and is certainly in many respects less trustworthy, although it is far from being an apparatus to be discarded.

The fifth method is that introduced by Strasburger. The pressure in the cuff upon the upper arm is gradually increased, while the observer palpates the pulse at the wrist and determines the point at which (and below which) the volume of the pulse is maximal. This method has gained great favor in Germany and upon it are based most of the more recent data of publications upon blood pressure. Its accuracy, at least in the hands of skilled observers, is vouchsafed by the tests of Brush, who found the error of careful estimations to be only 5 to 8 mm., and in my own hands frequent control with

the Erlanger apparatus entirely bears out his claims. This method has been in use in the Johns Hopkins Hospital during the past year, especially in the routine blood pressures made by the students;[1] the results of this general routine use have been far from satisfactory, so that students and internes have come to place no reliance upon it whatever. The reason for this discrepancy lies mainly in the lack of uniformity of pressure exerted by the palpating finger upon the radial artery. If it is possible for the observer to retain a perfectly uniform pressure upon the artery, the variations in the size of the pulse are readily appreciated, but if the size of the pulse under the finger is alternately decreased and increased by unsteadiness of the palpating finger, it becomes obviously impossible to determine when the pulse reaches its maximal oscillation.

It is very easy, however, to eliminate these variations in the pressure of the palpating finger by observing a simple precaution, by which this source of error may usually be eliminated even in the hands of those who have been in the habit of committing it in the highest degree. This precaution consists in simply *laying the tips of the index and middle fingers upon the lower end of the radius just lateral from the artery, and palpating the pulse with the balls instead of with the tips of the fingers.* Under these conditions variations of pressure by the fingers are exerted against the bone and not against the artery, and the main source of inaccuracy disappears.

There is, however, a further source of error not to be neglected, namely, that of inaccuracy in subjective perception. In order to minimize this it is necessary to disregard the first reading, using it merely to accustom the fingers to the changes in size which the pulse will undergo, and then to make at least five or six subsequent readings in order to eliminate the occasional errors of any single determination (which may be as high as 20 mm. Hg.). In a series of six determinations carefully made, at least four of them should give results within less than 5 mm. of each other, even when made by different individuals; and these results should be within 5 mm. of the results obtained by control with the Erlanger apparatus. Such has been my experience in the wards of the Johns Hopkins Hospital even when the determinations were made under my supervision by the very persons who had been obtaining the worst results with the Strasburger method. The pulse was felt by one person and the manometer (which he could not see) read off by another; the results were accurate if the above-mentioned precautions were taken.

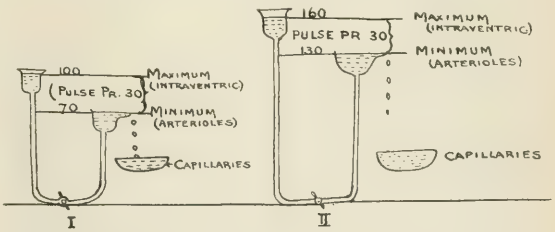
It is, therefore, clear that determinations of minimal blood pressure by the method of Strasburger may be of great value in the clinical estimation of blood pressure, particularly in the individual case in the hands of a careful practitioner; the maximal pressure may be fairly well estimated by the method of Riva-Rocci—with the broad Recklinghausen cuff. In general I have found that the readings by the method of Erlanger average about 5 mm. higher than the readings by digital palpation, though they sometimes coincide and are often 10 or even 20 mm. higher. The best results, therefore, possible for those observers who do not use the Erlanger apparatus, are obtainable by taking the minimal pressure by the method of Strasburger and the maximal by adding 5 mm. to the readings obtained by the method of Riva-Rocci (with the broad cuff). This will give in most cases results which may be quite uniformly accurate, and certainly comparable with each other, in the hands of one man, but very inaccurate in the hands of another less careful.

Determinations of this sort, therefore, though a legitimate aid to the practitioner who has reason to be certain of his own individual accuracy, should scarcely be used for published results. Unfortunately, the greater bulk of the work upon minimal pressures, especially by our German colleagues, is based upon these methods and subject to the fallacies discussed; in critical reviews of blood-pressure work the possibilities of these errors should be borne in mind.

Should the Minimal Blood Pressure be Expressed as a Fraction of the Maximal?

Another mistake of European observers consists in the expression of minimal blood pressure as a percentage of the maximal, somewhat regardless of the meaning of these quantities. This method of recording has crept into even such careful work as that of D. Gerhardt (l. c.). In general the maximal blood pressure represents approximately the intraventricular pressure, while the minimal pressure represents the algebraic sum of all the factors of resistance to outflow through the arterioles, viz., viscosity of the blood, arterial friction, breadth of bed, total-arteriole cross-section at the given instant. It is clear that the main resistance occurs not in the capillaries but in the arterioles which are most subject to the action of the vasomotors. As Dawson has shown, the minimal pressure is practically constant throughout the arterial system, at least as far as the saphenous artery in the dog, while the maximal falls gradually as the arteries become smaller; hence, at the very smallest arterioles, when maximal and minimal probably closely approximate each other we find both about equal to the minimal pressure in the aorta.[2]

The pulse pressure (the difference between maximal pressure and minimal pressure) then represents the difference between the greatest pressure in the aorta and the pressure in the arterioles; or in other words, represents the force tend-



[1] The pressure was gradually diminished instead of being gradually increased.

[2] The limits of experimentation prevent an accurate knowledge of the maximal and minimal pressures in arteries smaller than the saphenous of the dog, but these relations probably hold true in the main down to much smaller arteries.

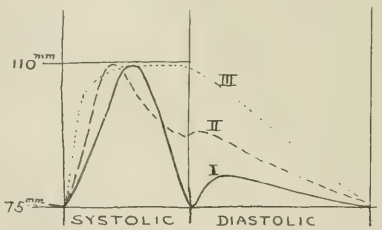
ing to drive the blood towards the periphery. The conditions at once become clear when we think of them in the light of the following experiment upon the model (Fig. 1). Let us suppose the maximal pressure (intraventricular pressure) is represented by a reservoir 100 cm. above the base or zero level, and that the minimal pressure is represented by a second reservoir (approximately the pressure in the smallest arteries and arterioles) only 70 cm. above the base, the two reservoirs being connected by a long rubber tube descending between them to the base zero, and closed by a revolving stop-cock. It is evident that the force driving liquid from maximal to minimal reservoir is equal to only 30 mm. of water, and the minimal reservoir must overflow before liquid flows out of it to a larger reservoir at a lower level arranged to catch such overflow (capillaries and veins). In this case the minimal pressure would be represented by 70 per cent of the maximal. Suppose the two reservoirs were raised to 160 and 130 cm., respectively, above the base. Their relations to one another would be unchanged, liquid would flow from one to the other at the same rate and hence would flow onward at the same rate to the venous system, but the percentage relation would here be quite different, being raised to 80 per cent or exactly what it would have been if instead of both being raised (the one from 100 to 160, the other from 70 to 130) the maximal pressure had fallen to 87 cm. and the outflow had diminished. Moreover, as has been shown by the experiments of Erlanger, Dawson, and Henderson, the pulse pressure is the correct measure of the volume of output of the heart under physiological conditions.

The absolute figures for the maximal and minimal pressures are of importance, but their relations expressed in percentages of the maximal pressure are very misleading. For example, with a maximal pressure of 220 mm. Hg. (from a case of chronic nephritis) a minimal pressure of 160 mm. would be expressed as 70 per cent, and would, therefore, be associated in significance with a maximum of 110 mm. and a minimal of 77 mm.—perfectly normal figures. Obviously the simple figures mean much more than the percentage, and the use of the latter should be discouraged.

The Dicrotic Pulse in Typhoid Fever.

Another point closely related to the study of the maximal and minimal pressures, particularly from the standpoint of Sahli's absolute sphygmogram (l. c.)[3] is the relation of pulse form to maximal and minimal blood pressures. This point has also been investigated by D. Gerhardt (l. c.), and especially by H. A. Stewart (10) in this laboratory. As the most interesting features and discussion of this problem will appear in the publication of the latter, it will suffice to mention here only the conditions present in the dicrotic pulse of typhoid fever. While serving as House Officer in the Johns Hopkins Hospital in 1903 to 1904, it was not infrequent for me to find either in the same patient at different stages of the disease or in different patients, maximal pressures of 110 to 115 mm. with minimal pressures of 75 to 80 mm. (determined with the Erlanger apparatus) both when the pulse was dicrotic and when the dicrotism had disappeared. The dicrotic pulse always corresponds with an extremely low dicrotic notch. In other words, as the dicrotic notch marks the end of the systolic period in the pulse (Marey (11), Huerthle (12)), the very low dicrotic notch indicates that the pressures in the aorta and in the more peripheral vessels have almost equalized themselves before the end of the period of systolic output, which is possible only in conditions of marked peripheral dilatation. Other signs of peripheral dilatation that clinically go hand in hand with the dicrotic pulse are the flushed face, the "bounding pulse," with rapid filling and rapid depletion of the arteries.

There are, of course, three forms of pulse curve possible, with the same maximal and minimal pressures (Fig 2):



I. In which the fall of the pulse is almost complete by the end of systole. This is the form of the dicrotic pulse.

II. That in which only about half the fall occurs during systole. This is the pulse of the normal individual.

III. The anacrotic pulse in which the rise is continuous throughout systole and the fall begins at the beginning of diastole.

It is clear from the foregoing that the first type represents the condition in peripheral dilatation and the last represents that in peripheral constriction, and this is further borne out by the work of Stewart. Evidently, therefore, the dicrotic pulse corresponds to the condition of maximal dilatation of both peripheral and abdominal vessels (the latter always present in typhoid) and yet nevertheless the maximal and minimal blood pressure is the same as in the second group of typhoid cases in which the dicrotic pulse is not present. Now it is evident that when there is peripheral vasodilation, the total arterial reservoir is increased and it is not unlikely also that the diameter of the aorta and larger vessels also is widened. (Since vasomotor nerves are present in the larger vessels; and since the carotid and other vessels of the dog may in the course of an experiment be seen to change their caliber by at least one-third, similar changes in the larger vessels in man are most probable.) But in order to fill a larger arterial bed with blood to the same head of pressure and to maintain the same pressure in diastole as in a smaller arterial bed, it is evident that a greater systolic output is necessary, and accord-

[3] The pulse curve plotted upon coordinate paper with the ordinate of maximal pressure at the summit of the curve, and the ordinate of minimal pressure just before the beginning of the next pulse wave.

ingly in cases with dicrotic pulses we usually have other evidences of increased heart action, ringing aortic second sound and strong cardiac pulsation—a fact to which my attention was called by Dr. Barker.

It might appear at first sight that the conception that the cardiac output with the dicrotic pulse is greater than is necessarily the case in the same patient after subsidence of dicrotism (and diminution of vasodilation) is at variance with the rules of Erlanger (l. c.), Dawson (13), and Henderson (14) above cited, that the pulse pressure is proportional to the systolic output. This rule is dependent upon the assumption that the diameter of the aorta is constant, which is no doubt the case in most normal individuals or in those where the vasomotor system is in tolerable equilibrium, but it certainly does not apply in all pathological conditions, especially where extreme peripheral dilatation is present. (The greatest discrepancy is found in experimental aortic insufficiency in which the pulse pressures may be multiplied at least four times with scarcely any change whatever in cardiac output, measured by Henderson's plethysmograph). (Stewart l. c.)

It, therefore, seems most in accord with the facts to conclude that the dicrotic pulse of typhoid fever is the result of the coincidence of very marked peripheral dilatation with somewhat increased heart action, and that it may disappear with the subsidence of either of these factors.

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SOME VARIATIONS IN THE FORM OF THE VENOUS PULSE.

A PRELIMINARY REPORT.

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(*From the Physiological Division of the Medical Laboratory.*)

Since the publications of James Mackenzie (1) have made the forms of the venous pulse well known, there has been little tendency among writers upon the subject to differ as to the form of the physiological venous pulse, although quite recently Bard (2), of Geneva, has published a series of tracings from normal individuals which do not coincide exactly with those of the former. Bard finds present in his tracings a small wave intermediate between the presystolic (auricular) wave and the carotid wave of the venous pulse, and concludes that this wave is due to the systole of the ventricle in the interval before the aortic valves have been opened. I have frequently noticed in my own tracings that the so-called (*c*) wave ascribed by Mackenzie to the transmitted pulse from the carotid occurred at an appreciable interval before the carotid pulse (as much as .05 sec. or about the time necessary to open the aortic valves) and can fully agree in Bard's interpretation,[1] as against Mackenzie's. Mackenzie's view has, moreover, been absolutely refuted by the beautiful tracings obtained by Morrow (3) upon animals, in which the carotid has been ligated both centrally and peripherally without diminishing the size of the (*c*) wave, and it is further borne out by the exactly similar tracings obtained from within the auricle itself. I have never, however, been able to obtain tracings resembling those of Bard in which this systolic wave appeared not merely

[1] In fact I had given the same explanation of this wave in a paper read before the Johns Hopkins Medical Society on February 19, 1906, and published in the American Journal of Medical Sciences in September, 1906, a little later than Bard's paper.

as the beginning of the slope to the carotid wave, but quite distinct from it. Bard, moreover, finds a similar splitting of the postsystolic or (*v*) wave (whose crest is marked by the opening of the tricuspid valve) into two varying waves which he designates by the letters (*d*) and (*f*). Undulations upon the surface of the (*v*) wave are not infrequent but are far from being the rule, and the tracings published by Bard, although representing a different, and perhaps better, technique than usually employed do not accord well in these regards with the best tracings by other observers.

following the *v* wave, and at the end of the subsequent rapid filling of the vein, and gives rise to a small elevation closely resembling that produced by an auricular contraction, providing the latter were not followed by systole of the ventricle. This condition might well be present providing there were disturbances of conductivity, but in neither of the cases in which the phenomenon has been observed were any other signs of disturbed conductivity present; the conduction time (*a-c*) interval was normal and there was no bradycardia. It is true that frequently the conductivity for an auricular ex-

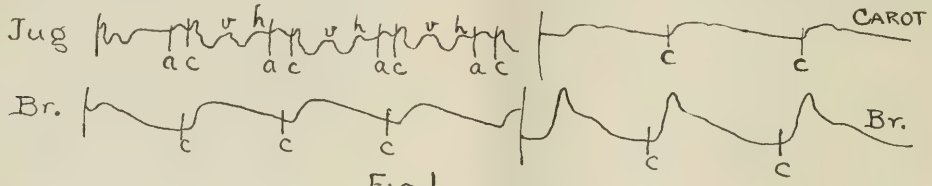

Fig 1.

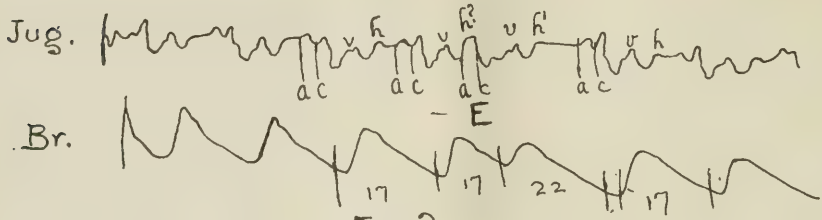

Fig 2.

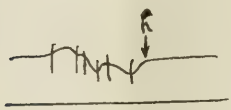

Fig 3.

Fig. 1.—*Jug* = pulse from jugular vein; *br* = pulse from brachial artery; *carot* = pulse from carotid artery; *a* = auricular presystolic wave; *c* = time of occurrence of wave in carotid artery; *v* = postsystolic wave, the crest of which marks opening of tricuspid valve; *h* = wave during diastole; from a patient with myocardial disease.

Fig. 2.—From same patient after exercise, showing extrasystole at *E*, probably auricular in origin. Lettering as in Fig. 1, Arabic numerals refer to space in mm. between successive pulse waves in brachial pulse.

Fig. 3.—(After Morrow.) Tracing from jugular vein of a dog, showing shoulder (*h*) upon curve during diastole, corresponding to wave (*h*) in human venous pulse. Only a part of Dr. Morrow's figure is reproduced.

From the above mentioned facts it is evident that great variations occur in the form of the venous pulse of different individuals, although in the main they adhere quite closely to the conventional type as described by Mackenzie. Recently, however, I have occasionally encountered a slight variation of form occurring in the diastolic portion of the cardiac cycle, which might well be confounded with disturbances in conduction or with auricular extrasystoles, and which therefore merits attention.

The wave referred to (Fig. 1, *h*) occurs after the collapse

trasystole is less than that for the regular beats, but as shown by Hirschfelder and Eyster (4) this applies only for early extrasystoles occurring well within the first third of the cardiac cycle, and does not apply to the period when the wave under consideration is produced. This reasoning justified exclusion of the auricular extrasystole in the first case in which this unusual wave was encountered, and in which the question of disturbed conduction was one of great importance to the patient. That it could not indicate a true partial block was

shown by the fact that the wave was not exactly midway between the two definite auricular contractions.

On another occasion, after vigorous exercise an extrasystole took place at exactly the time of the wave (Fig. 2). This extrasystole was followed by ventricular contraction and after the extrasystole the same wave Fig. 2 (*h*) occurred in exactly the same portion of diastole, without any relation to the auricular waves, and without further disturbance of the cardiac rhythm. This in itself, as well as the subsequent occurrence of the same wave in a perfectly healthy individual with perfectly normal heart seems sufficient to justify the conclusion that it is to be regarded as an event in the normal diastole, more pronounced in some hearts than in others.

It will be noticed that in the very excellent tracing obtained by Morrow (3) from the jugular vein of a dog (reproduced below, Fig. 3,) that just at this point in diastole there is a very suggestive elbow upon the pulse tracing (*h*), and this point corresponds to the end of the most rapid stage of filling of the veins after the ventricle has been filled. This joint corresponds more or less to the time at which the cardiac plethysmograph shows that the main filling of the ventricle has occurred (Henderson), and at the time when, according to Henderson (5), model experiments show that the mitral and tricuspid valves are closed by the floating together of the cusps. Whether or not this wave is actually produced by the floating together of the cusps, and whether such a forcible undulation may be responsible for the third sound of protodiastolic gallop rhythm cannot at present be stated.[2] In the first case observed, the heart sounds were extremely distant, and no note of the gallop rhythm was made during his entire stay in the hospital. In the second case, the heart sounds were loud and clear, but at the end of expiration a very faint third sound coinciding with the time noted in protodiastolic gallop rhythm was audible in the tricuspid area, at the time the venous pulse was taken. This sound was not loud enough, however, to be definite, and none of the tracings which I have made at other times upon cases with gallop rhythm have shown this peculiar variation; so that as yet no definite conclusions as to the relations of this unusual wave of the venous pulse to either the closure of the tricuspid valve or the gallop rhythm are warrantable.

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THE RAPID FORMATION OF ENDOCARDITIC "VEGETATIONS."

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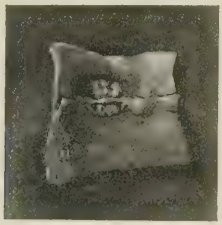
The cauliflower-like form assumed by the vegetations of verrucose endocarditis has always been a matter of some interest and curiosity to both pathologist and clinician, and it has been customary to assume that the unevennesses in these warty outgrowths were brought about by the more or less unequal contraction of the organizing fibrin along the strands of Zahn. Undoubtedly this mechanism does play a large and important rôle in the formation of endocarditic vegetations, but, in some cases at least, the form of the latter may already be determined in the thrombotic deposit which collects upon the valve immediately after the production of the lesion. This became most strikingly apparent in the experiments upon artificial aortic insufficiency in the dog, performed by Dr. H. A. Stewart and myself during the past winter. The lesions of the valve were all produced either by means of a blunt button-pointed probe or by a MacCallum valvulotome introduced through the left carotid and thrust through the aortic valve. In every case the heart responded, after a few beats, by a marked fall in the minimal blood pressure, with little or no change in the maximal;[1] and the character of the pulse became collapsing. In a few of the experiments it was observed that about an hour later the minimal blood pressure again rose to near normal, and the collapsing character of the pulse disappeared. At autopsy in these cases it was found that the puncture through the valve had become plugged with fresh yellow fibrin and blood-platelets, which in one instance had assumed definite cauliflower-like outlines (as shown in the figure). This "vegetation"—really a thrombotic deposit—was absolutely fresh and non-adherent; the lesion to the valve

[2] Since the above has gone to press Theobald (Deutsches Arch. f. klin. Med., Leipz., 1907, XC, p. 85, Fig. 13) has published a veinous tracing from a dog, showing a definite *h* wave after vagus stimulation. On the other hand, experiments with dead hearts have thrown some doubt upon Henderson's view that the auriculo-ventricular valves close during diastole.

[1] Stewart, H. A. An Experimental and Clinical Study Upon the Pulse and Blood Pressure in Aortic Regurgitation. Thesis, University of Edinburgh, 1907. To be published later.

had been produced only one hour before and there was absolutely no sign of previous lesion. The mass itself consisted of



"Vegetation" of Fresh Fibrin One Hour After Puncture of Aortic Valve.

a soft homogeneous yellow thrombus and, on handling even gently disintegrated like any other *intra vitam* clot, leaving no trace of organized material. The interesting features connected with it are two-fold: First, the rapid formation of plugs in the freshly formed holes in the valves, sufficiently firm temporarily to repair the damage. Such a rapid temporary repair may play a large part in the recovery from spontaneous rupture of an aortic valve after over-exertion, and perhaps also in staying the course of the leak in acute endocarditis. Secondly, since the soft fibrinous vegetation in the course of its formation had already assumed the verrucose form, this could not be the result of contraction of strands of tissue, but the fibrin was probably deposited in the stalk-like forms by the to and fro current of the blood passing through the valve, other irregularities being most likely the result of eddy currents. In the permanent vegetation this form would of course be modified largely by the subsequent contraction of the "organizing fibrin," although the resemblances of these fresh fibrinous deposits to the usual form of vegetation found in aortic insufficiency renders it possible that this modification of form is not as great as might be supposed.

THE CALCIUM, MAGNESIUM, PHOSPHORUS, AND NITROGEN METABOLISM AND THE ORGANIC ACIDITY OF THE URINE IN A CASE OF SO-CALLED PHOSPHATIC DIABETES, WITH COMMENTS UPON AN INTERESTING FORM OF ACIDOSIS.

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In 1876 L. J. Teissier described a number of cases which had much in common from a clinical standpoint. The principal symptoms were polyuria, very acid urine of high specific gravity and increased excretion of phosphates in the urine. Some of the patients suffered from nervous symptoms. In another group of his cases glycosuria with all the typical symptoms of diabetes developed, and cataracts were often found. For this latter reason Teissier thought it justifiable to call this symptom-complex "*phosphaturie à forme diabétique.*" By doing so he created a new form, "essential phosphaturia," which he distinguished from phosphaturia in the sense known at that time, viz., the excretion of turbid urine due to the precipitation of phosphates. Later Ralfe, in the London Lancet of 1887, referring to the original article of Teissier, confirmed the findings of the latter by describing a few more cases of this kind. On going over the literature of phosphorus metabolism we have found this "phosphatic diabetes" mentioned frequently by investigators.

Recently Dr. H. Greenbaum, of Baltimore, sent one of his private patients into the Medical Clinic at the Johns Hopkins Hospital with symptoms resembling very closely those described by L. J. Teissier as characteristic of phosphatic diabetes.

The patient, a Jewess, 39 years of age, complained of headache, occasional stiffness below the right knee, itching of the skin, dryness and cracking of the skin, hyperacusis, constipation, susceptibility to colds and increased frequency of urination.

The family history is negative except on the nervous side. Several members of the family have been excitable. One uncle died in an insane asylum and one cousin was also insane. The patient's father was a nervous man, dying at 63 of some form of paralysis.

As a child she had measles, but remembers no other illnesses. She married 21 years ago. About 12 years ago the patient lost some 12 pounds in weight in the course of a short time, suffered from cracking of the heels and from boils on the body and from infected finger tips. She consulted Dr. Osler, who found the urine of high specific gravity but it contained no sugar. Her appetite was ravenous and her thirst marked. She complained of sinking spells, during which she would become dizzy and things would look black to her, though she did not fall. She suffered from great weakness. She often felt chilly when others were quite comfortable. As the patient was going to Europe, Dr. Osler referred her to Dr. von Noorden, who in turn sent her to Carlsbad under

the care of Dr. Kraus. There the patient took the waters (Carlsbader sprudel) and was given electrical treatment. She remained in Carlsbad for six weeks and later spent three weeks in St. Moritz, where she improved generally. The boils disappeared and the heels were better.

The patient has given birth to ten children and in addition has had four miscarriages, though no evidence of lues in her or her family could be found. The living children are all healthy. She has had some local gynæcological lesions which have been treated surgically. At the menstrual period she has headache, pains in the legs, is nervous, irritable, and tends to lose control.

During the past twelve years the patient has had periods of improvement alternating with periods when the symptoms were prominent. A year ago she suffered much from cardialgia. When her symptoms are worse the itching is troublesome, especially under the chin, on the chest and under the breasts. The skin often becomes hyperæmic at these times. When her symptoms are marked the frequency of urination is increased. During the past three months the patient has noticed falling of the hair. A feeling of constant pressure on the top of the head is complained of. She sleeps very poorly and tires easily.

The appetite is good. There is no cough or dyspnœa. She wears glasses prescribed by Dr. Friedenwald for her "eye-strain."

On examination the woman was found to have a large frame and to be rather over-nourished, weighing 177 pounds. The skin is pale and the lips slightly cyanotic. Tongue clean. No jaundice. Pupils active. Eye-muscle movements good. Pulse 21 to the quarter, regular in force and rhythm. Radial just palpable. Epitrochlears not enlarged. No enlargement of the lymph glands of the neck. Heart and lungs normal. Lower pole of right kidney palpable; left not felt. Sigmoid palpable. Abdomen otherwise negative. Knee-kicks active and equal. No clonus. No œdema of the ankles. No relaxation of the sacro-iliac joints. The blood was normal.[1]

The urine on examination showed high specific gravity (1030) in spite of the polyuria (2-2½ l.) very great acidity (1500), remarkably large output of nitrogen (27 gms.) and P_2O_5 (5.7 gms.); uric acid normal (0.4 gms.).

As a careful metabolic study of such a case has never been made before we thought it interesting to undertake this work. The patient came to the hospital for eight days and was put for the whole period on the Folin diet, a purin-free food consisting of 119 gms. of protein, 225 gms. of carbohydrates and 148 gms. of fat. It was greatly to our advantage to use this diet, for Folin in his admirable investigation of the composition of normal urines employed it in order to set up normal standards for the urinary constituents. Comparisons, therefore, with the figures he obtained, facilitate the explanation of pathological findings. The water intake was kept constant for the entire period, a factor which, of course, has an influence on the urinary excretion. The experiment was divided into three periods:

Period I preceded the time when the patient came to the hospital. The urine of a number of days was saved (for each 24 hours) at the patient's home and sent the same day to the laboratory for examination. It was not possible during this period satisfactorily to control the patient's food. This was however accomplished during the eight days of the second period, spent in the hospital.(*Period II*). In *Period III* the patient was at her home again and the total amount of urine was collected as in *Period I* for a few days.

From the findings in the patient's urines previous to admission to the hospital it was clear along which lines the metabolism experiment should be directed. There was a hyperacidity of the urine with high phosphoric acid excretion. The question presented itself, to what is this increase in acidity due? Is it dependent on the presence of large amounts of acid salts, or to an increase in the organic acids? The possibility of having to deal with free mineral acids was ruled out *a priori;* they never occur free in the urine. Besides the acidity of the urine, the total nitrogen (method of Kjeldahl) the ammonia (Folin), the P_2O_5 (Volhard), the calcium oxide and magnesium oxide (gravimetrically by precipitation as calcium oxalate and magnesium ammonium phosphate, respectively) were determined.

The organic acids (free and in the form of the neutral salts) were carefully estimated. In regard to the method used for the organic acids it may not be out of place to say a few words of explanation. Magnus-Levy in his investigations on the amount of organic acids in the urine of diabetic individuals used a very complicated method which was until a few years ago the only available one for this purpose. It consists in determining separately on one side all the inorganic bases (potassium, sodium, ammonia, calcium, magnesium), on the other side all the inorganic acids (HCl, H_2SO_4 and H_3PO_4). Both are reckoned in terms of acidimetric units. By subtracting the value of the bases from the value of the acids there is always found a small excess of bases which can be due only to the presence of organic acids. These organic acids are combined with the excess of inorganic bases. Under normal circumstances uric acid and hippuric acid are probably the most important organic acids. Magnus-Levy's method does not take into account any organic acids, which might be present in the urine as free acids and not in the form of neutral salts. Such a possibility is not at all ruled out by any of the work done on the acidity of the urine. Folin is very

[1] The patient was also studied at one time by Dr. Thomas R. Brown of Baltimore, who found a high acidity of her urine. Dr. Brown mentions this case in his article on "Urinary Hyperacidity, a Consideration of Cases with Symptoms Suggestive of Cystitis, but with no Infection due to this Cause." In this interesting paper, the author describes over ten cases, all neurasthenic women. The urine, when tested for the acidity gave always extraordinary high results. As soon as the patients were put on a rest cure and alkalies were given with the food, the symptoms disappeared rapidly. Brown warns against treating such patients for cystitis, as deplorable results may follow. He does not attempt to explain the high acidity of the urine, but is rather in favor of the view that the cause does not lie in the diet and that some pathological condition of the nervous system is responsible for the hyperacidity.

much in favor of admitting the presence of free organic acids in certain pathological urines. As the organic acids are very weak acids, the inorganic bases will combine first with the stronger inorganic acids (sulphuric, hydrochloric, phosphoric acid), and only if there be an excess of bases, are these latter used to neutralize the organic acids. The method used by us in the course of the present investigation was described

	Food.				Urine.												Feces.			
	N. in gms.	P_2O_5	CaO.	MgO.	Vol.	Sp. gr.	N.	NH_3 ratio.	P_2O_5 mineral.	P_2O_5 org.	CaO.	MgO.	Fixed Alk. $\frac{N}{10}$ in cc.	Total Acidity.	Org. Acids in cc. $\frac{N}{10}$	Weight in gms.	N.	P_2O_5	CaO.	MgO.
Dec. 1.....	17.6	3.75	2.53	.348	900	1030	27.2		5.71											
" 3.....	17.6	3.75	2.53	.348	2250	1020	31.2		3.31		.33		−902							
" 5.....	16.9	3.84	2.64	.349	2125	1030			3.23		.765		−469							
" 8.....	16.9	3.84	2.64	.349	3000	1020	24.6		2.86		.711		+ 64							
" 16.....	15.2	3.87	1.81	.179	2100	1030	19.8		2.71	.40	.684	.109	− 978	535	593	19	.91	.56	.19	.08
" 17.....	15.2	3.87	1.81	.179	1650	1030	16.4	3.7	3.39	.25	.563	.110	− 901	754	982	35	1.37	.83	.49	.17
" 18.....	16.1	2.97	2.14	.268	1740	1030	15.3	3.8	3.05	.09	.347	.201	− 226	748	974	26	.60	.64	3.88	.09
" 19.....	16.1	2.97	2.14	.268	1430	1030	16.6	4.0	3.07	.09	.334	.157	+ 316	689	847	11	.60	.34	10.08	.05
" 20.....	15.2	3.87	1.81	.179	1650	1030	16.1	4.1	3.07	.40	.358	.177	163	697	1263	95	4.23	3.15	.15	.08
" 21.....	15.2	3.87	1.81	.179	1800	1030	17.8	6.0	2.92	.25	.268	.161	687	684	631	13	.57	.39	1.04	.09
" 22.....	16.1	2.97	2.14	.268	1770	1030	14.6	5.1	2.88	.17	.298	.161	−400	655	779	66	3.48	1.76	1.64	.59
" 23.....	16.1	2.97	2.14	.268	1815	1030	14.9	4.9	2.96	.09	.349	.147	− 87	664	203	44	1.61	1.12	2.55	.50
Jan. 29.....					2300	1030	14.9	5.1	2.67	.02	.676	.197	−449	621	1107					
Mar. 5.....					22	1540	15.3	5.8	2.95				+ 653	108	828					
" 12.....					30	2000	19.3	1.4	1.98				+ 668	220	1224					
" 26.....					35	1535	17.4	2.6	2.33					468	727					
Apr. 16.....					1830	1030	8.4	11.2	2.43				+ 933	382	942					

by Folin in 1903 and modified by E. S. Edie and E. Whitley in 1906. The last two authors do not mention Folin's work and appear to regard the method as a new one. The procedure is as follows:

A. A portion of the fresh urine is titrated after saturation with crystallized potassium oxalate against the decinormal sodium hydrate solution, phenolphthalein being used as an indicator.

B. In a second portion of urine the ammonia is determined by Folin's second method.

C. A third portion is evaporated to dryness in a platinum crucible and incinerated, care being taken not to heat the crucible to more than a dull red heat (to avoid loss of sodium and potassium). By this incineration all the organic acids with the organic basic constituents of the urine as well as the ammonia are volatilized, leaving behind only the inorganic constituents. By dissolving the residue in water and titrating in exactly the same way as was done with the fresh urine one finds the inorganic acidity (leaving NH_3 out of account), that is to say, the bases liberated by volatilizing the organic acid formerly combined with them. In burning the urine the ammonia, which is one of the inorganic bases, is removed. A separate estimation of this base becomes therefore necessary. By adding this value to the alkalies measured after incineration we obtain the actual mineral acidity. This latter is subtracted from the total acidity A and gives the organic acidity, i. e., the organic acids present in the urine as salts and in the free state. For all details and theoretical discussion of urinary acidity we refer to Folin, Hoeber, Edie, and Whitley. This method yields reliable results when every precaution is taken. The use of this method in a number of other investigations carried out in the laboratory here always proved satisfactory.

	Nitrogen in gms.	Total P_2O_5.	CaO.	MgO.	Remarks.
Dec. 16..	+0.33	+0.49	+1.75	+0.162	
" 17..	+0.97	−0.47	+0.99	+0.65	
" 18..	+0.66	+0.14	−1.59	+0.52	
" 19..	+0.30	+0.41	−7.77	+0.139	
" 20..	−6.80	−2.20	+1.29	−0.079	Patient gets 3 tablets of thyroid extract.
" 21..	±0	+0.60	−0.47	−0.078	
" 22..	−2.2	−1.72	+0.26	−0.486	
" 23..	−0.4	−0.84	−1.08	−0.446	Patient gets $CaCO_3$ gr. xxx, ad doses IV (8 gms.).
Total ...	−6.14	−2.75	−6.62	−0.67	

Discussion of Results.

Phosphorus metabolism.—Teissier and Ralfe determined the phosphates in their cases as calcium and magnesium phosphates respectively. The figures obtained are not at all a true index of the phosphoric acid present because of the varying composition of the precipitates. Another point is that the phosphorus in the food and feces was not taken into consideration. It is only from a study of the complete balances, i. e., the content of phosphorus in the food, as well as in the urine and feces that we can hope to find out any irregularities in the metabolism of this element. From a number of very thorough investigations we know that phosphorus is retained by the organism more eagerly than any other substance. The reason becomes evident when one thinks of the wide distribution of the phosphorus in the human body, as a constituent of bone in inorganic combination, and as a component of the cell nucleus, and of the blood. The phosphates of the blood are of the highest importance for the maintenance of the

alkalinity of the blood. From experiments made by Walter on dogs and recently by Fitz and Alsberg on rabbits, it is known that the ingestion of mineral acids produces increased output of phosphoric acid in the urine. In severe cases of diabetes the phosphoric acid excretion is found to be increased. Administration of alkalies seems to prevent the loss. All this suggests that a production of acids within the body or their administration might result in an increased elimination of phosphoric acid. There is good evidence that the disodium phosphate of the blood gives up one atom of sodium to neutralize the acid produced; as a consequence the proportion of the different constituents of the blood is changed and the organism tries to reestablish the normal equilibrium by excreting the excess of acid phosphates formed. One would expect, therefore, to get high amounts of urinary phosphoric acids in pathological conditions in which an acidosis occurs. The urine of the days of Period I contained an exceptionally high output of phosphoric acid. The patient was very nervous during this period and all the symptoms were pronounced. Unfortunately, on beginning the complete study of metabolism in Period II the patient improved so rapidly that nothing unusual was found in the output of total phosphates. The slight retention of phosphorus observed could perhaps be explained by the composition of the food, which contained a rather high percentage of this substance, or by an attempt on the part of the organism to replace the possible loss during the period preceding the experiment.

A remarkable feature is the relatively high percentage of organic phosphorus. Symmers found that in normal urine the amount of organic phosphorus never exceeds 2.5 to 4 per cent of the total phosphoric acid. On the first day of Period II the organic phosphorus is as high as 15 per cent of the total. It decreases then rapidly and only on the fourth and fifth day is there again an increase to be noted. Neither thyreoid feeding nor the administration of calcium carbonate seems to influence the output of phosphoric acid. Of course we realize that the time of observation was very short and that inferences must be cautiously drawn. In the period after the patient had left the hospital the phosphorus excretion was very much diminished, probably as a result of the administration of alkalies during this period.

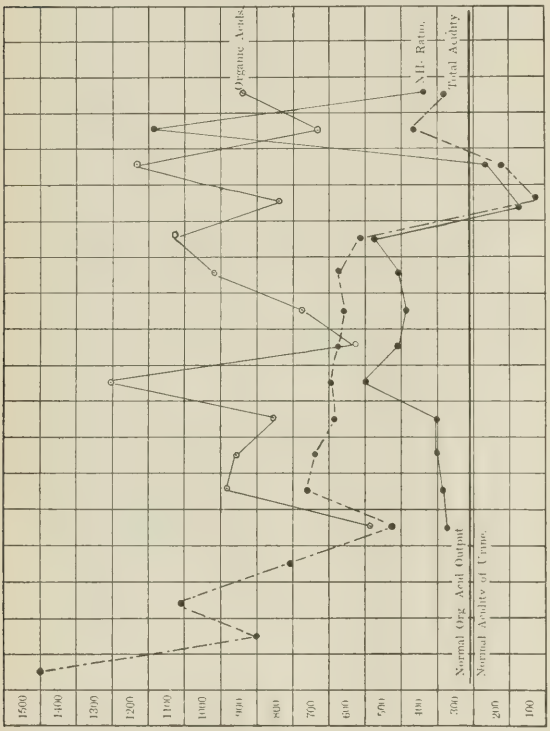
Nitrogen metabolism.—In Period I the nitrogen-excretion by the urine is extremely high, maximum 31.2 gms. We do not think that this can be due altogether to a correspondingly high intake in the food. As the patient is always losing weight during the time when the symptoms become more pronounced this high nitrogen-excretion might partially be accounted for by the breaking down of tissue. In Period II the patient was practically in nitrogen-equilibrium during the first four days. The thyreoid tablets produced a marked increase of nitrogen in the urine for one day only. The loss of nitrogen in the days following the thyreoid administration was very slight. Nothing abnormal can be noticed in the nitrogen excretion of Period III, except the relatively low excretion on March 26, a day when the patient's general condition was worse. This may be explained by the partial loss of appetite that sometimes accompanies deterioration of the patient's general condition.

Calcium metabolism.—Large amounts of calcium oxide characterized the analyses of the urines of Period I, the maximum being 0.76 gm., whereas normally not more than 0.5 gm. is excreted daily on a mixed diet. At the beginning of Period II the calcium oxide is still high, 0.58 gm. being 21 per cent of the calcium oxide in the food. Voit gives the percentage of calcium oxide in normal urine as 10 per cent of that in the food. In regard to the distribution of calcium oxide in the urine and feces during this period it may be said that 88 per cent was found in the feces and 12 per cent in the urine. This indicates either that there is a large excretion of calcium through the intestinal wall or the calcium of the food is not dissolved to any great extent. As the absolute amount of calcium oxide in the urine in comparison with the calcium content of the food is large, one would be inclined to think that the excretion of calcium through the intestine might be the cause of the large amount of calcium oxide in the feces. Our knowledge of pathological, as well as of physiological calcium metabolism, is still very incomplete. It is only in recent years that thorough studies of calcium balances have been carried out, and additional work is required first of all to establish standards under normals conditions, as they would be of great help in interpreting the findings in pathological cases.

Magnesium metabolism.—Nothing abnormal was detected in the metabolism of magnesium. Of the magnesium found to be excreted in our case 50 per cent passed through the kidney and 50 per cent through the intestines.

The acidity of the urine.—By consulting the chart illustrating the changes in the amount of organic acids, the total acidity and the ammonia ratio it will be seen that all of them show great deviations from the normal. The total acidity in Period I was remarkably high, from 1500 to 800 cc., the normal value being 300. In Period II no great changes occurred, the average value being about 700, being still more than twice the normal. After January 29, alkalies in the form of sodium bicarbonate were given to the patient and the effect was pronounced. The total acidity decreased within one day so as to be even below the normal. In spite of the administration of alkalies by the mouth, however, the total acidity showed a strong tendency to rise after March 1, and at this time the patient's condition was becoming gradually worse. On April 16 the total acidity was again low, apparently the result of a rest cure taken by the patient in Atlantic City. The organic acids in the urine increased to about 3 or 4 times the normal quantity. Unfortunately the urine of Period I was not examined for organic acids, but there is sufficient evidence from the results of the second and third period to point to a highly increased output of organic acids in that period also. In regard to the acidity another point of interest lies in the ammonia ratio. Some days the latter was very much increased (11 per cent), on other days the ratio was quite normal. After administration of alkali the ammonia is replaced by the alkalies and the ammonia ratio becomes therefore very much

diminished. The question whether the absolute amount of ammonia in the urine or the percentage of the total nitrogen represented by ammonia-nitrogen should be regarded as the index of acidosis is still open to discussion. Friedrich Müller is in favor of the former as a diagnostic measure. Schittenhelm and Katzenstein in a series of 12 experiments came to the conclusion that the ammonia ratio gives a truer picture of the degree of acidosis. In our opinion both factors may be of value. In a pronounced acidosis, as in diabetes where clinically all the symptoms point to acid intoxication one will always find a high output of ammonia in the urine, amounts of two or more grams. The ammonia determination



by itself will remove any doubt in such cases, but in a beginning acute or in a chronic acidosis the ammonia ratio may yield a more helpful result. Thus, for example, should the nitrogen metabolism be very low, as a result of fasting or of an abnormal diet containing only a little protein, the total nitrogen excretion may be much lower than that of a normal person and the ammonia be within normal limits; an acidosis would not be detected by an ammonia determination; if we were to determine the ammonia ratio in such a case, however, we would find out immediately that the latter is largely increased as contrasted with the normal and we should be perfectly justified in saying that an acidosis existed.

We may conclude, therefore, from the data obtained in the course of this investigation that in the case under consideration we had to deal with urinary symptoms that are certainly due to a pathological metabolism which manifests itself in the excretion of a relatively large amount of organic acids in the urine, accompanied by a hyperacidity, an increased excretion of organic phosphorus compounds and a somewhat abnormal calcium metabolism. The results suggest that we had to deal also with a pathological increase in the phosphates in our case, as Teissier asserts for his cases of a similar type, but we have not found sufficient evidence to establish firmly this supposition.

What was the cause of this acidosis? A short review of the knowledge of acidosis, or as it is sometimes called, acid intoxication, may help us to answer this question. Acidosis can be produced in normal individuals by a change in diet or by starvation. It is well known that on putting a man or an animal on a diet free from carbohydrates, acetonuria develops in the course of a few days. The same is true in simple fasting or starvation. The cause of the production of acetone, which is derived primarily from diacetic acid and β-oxybutyric acid has been found to be the restriction of carbohydrates in the food. It seems that carbohydrates play an important rôle in the oxidation of intermediary products of metabolism, especially those of the fats. It was Rosenfeld and Hirschfeld's fundamental investigation that demonstrated this relation. A clearer insight into the cause of diabetic acidosis was derived from the work of these authors. In diabetes as a result of a specific morbid condition the carbohydrates are not at all (or in milder cases only to a limited extent) available for the oxidation of these intermediary products of the fats (and possibly of the nitrogen-free carbon chains of the deamidized amino-acids which result from protein-cleavage), and, therefore, the urine contains acetone, diacetic acid and sometimes β-oxybutyric acid.

In many other diseases, e. g., in typhoid, scarlatina, pulmonary tuberculosis, carcinoma, in diseases of the stomach and intestines, epilepsy, eclampsia of pregnancy, diacetic and β-oxybutyric acid are sometimes present in the urine. In most of the reports on the subjects no attention is paid to the diet of the patient. It was v. Noorden who first pointed out the fact that insufficient ingestion of food may be the cause of acidosis in febrile diseases. As a matter of fact, acetone is never found in the early stages of febrile disease while the diet is still normal and there has been no lack of carbohydrate-ingestion. Further careful work must decide whether or not an abnormal metabolism is the cause of the appearance of these acids in the diseases above mentioned.

In many other morbid states diacetic acid and β-oxybutyric acid are occasionally met with in the urine. Becker described a toxic acetonuria due to disintegration of albumin and lack of oxygen, the latter being attributed to the destruction of red blood corpuscles. As an example he mentions poisoning with carbon monoxide. Recently Friedrich Mueller in a lecture on an obscure form of acidosis and acid diathesis, delivered at the Baltimore Clinical Society, stated that often in the urine

of patients presenting a sediment of uric acid crystals, he could by the method of Magnus-Levy for the determination of organic acids in the urine demonstrate that, in spite of the acid reaction of the urine, a large excess of inorganic bases was present, a finding which he could explain only by assuming the presence of an excess of some organic acid. No acetone or diacetic acid or lactic acid could be detected in these urines.

Coming back to the consideration of our case it looks as if the findings of Friedrich Mueller corresponded in many respects with ours. We were never able to demonstrate the presence of acetone, diacetic acid, or lactic acid in the urine. Furthermore, the patient's tolerance for carbohydrates was tested by her family physician, Dr. Greenbaum, who has kindly turned over to us the results of his test. The patient was given 150 gms. of sugar and the urine examined on the two following days for sugar. No reducing substance could be found. The possibility that we had to deal in this case with a disturbed carbohydrate metabolism is therefore ruled out. Millon's reagent yielded a slightly positive reaction in all the specimens examined. But tyrosin or any other oxyphenyl-containing acid alone cannot account for the considerable increase of the acidity observed. Another investigation will have for its purpose the isolation of the acids concerned, and we hope later to be able to gain more accurate information regarding their nature and source. The suspicion that the thyreoid gland could be involved was ruled out by the normal action of the patient after thyreoid feeding.

The question presents itself: Could this increased excretion of organic acids explain any of the patient's symptoms? It is not impossible that even such a comparatively moderate increase in the acidity of the urine might cause a decrease in the blood or tissue alkalinity by washing out valuable alkalies from the organism. The removal of calcium seems to have a special influence on the nervous system. Sabbatani in studying the biological action of calcium salts on the nervous system found out that the small amounts of calcium contained in nerve tissue has a moderating influence on the sensibility of the nerves. Removal of calcium salts from the nerve cells increases their irritability to such an extent that convulsions can be produced resembling those observed in epilepsy. Ronconi, a pupil of Sabbatini, as a practical application of the findings of his teacher, used subcutaneous injections of calcium bromide in the treatment of epileptic attacks.

Quest analyzed seven brains, two of them fœtal, five of them brains of children varying in age from one month to eight years; he noticed that the calcium content of the brain of the fetus and new-born child is strikingly high in comparison with that of the brains of older children. The examination of two brains of children dead of tetanus revealed a very low calcium content. The studies of W. H. Howell and of Jacques Loeb on the necessity of an equilibrium among the cations of the blood and tissue juices are very interesting. At least there are indications that calcium plays an important rôle in the functions of the nervous system. This could perhaps explain the fact that whenever an acidosis is marked the nervous system becomes more or less involved. It is fascinating as an hypothesis to think of some of the functional neuroses and psychoses, hitherto spoken of as being "without organic basis" as maladies which ultimately may be proven to depend upon "an inorganic basis," viz., a disturbance in mineral metabolism.

Conclusions.

In a case of so-called phosphatic diabetes, the study of metabolism revealed the following facts:

1. The patient excreted a urine of very high acidity, due to the presence of abnormally large amounts of organic acids, the exact nature of which has not been determined thus far, though the latter point is still under investigation.

2. The patient's carbohydrate metabolism was found to be normal, so that the existence of a larvate diabetes mellitus is ruled out.

3. Whether the appearance of the organic acids in the urine is due to (a) an overproduction compared with the normal amount, or to (b) a lack of oxidation of these intermediate products of metabolism, or whether both factors are concerned, we do not know. It may be asserted, however, that the increased output of organic acids in the urine certainly depletes the body of alkali. It is probable that the cases described by T. R. Brown would, if similarly investigated, present a similar metabolism. It seems probable, too, that a number of the cases with the same clinical symptoms described by Teissier and Ralfe would have presented similar features in regard to acidosis, had they been examined therefor.

4. Whether it is that the abnormal symptoms on the part of the nervous system presented by the patient are the result of acidosis or that the metabolism of the individual is so disturbed by the pathological action of the nervous system, as to tend secondarily to an increased excretion of organic acids, cannot be decided at present. One fact that seems to us well established by both clinical observation and metabolic study is that acidosis is closely connected with nervous disturbances.

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A STUDY OF THE METABOLISM IN A CASE OF SO-CALLED "ARTHRITIS DEFORMANS."

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The object of the investigation, the results of which are included in this paper, was to study, under the influence of a diet the constituents of which could be accurately known and controlled, the pathology of so-called "arthritis deformans" from a chemical standpoint.

Literature.—The history of the development of our chemical knowledge concerning the morbid processes in arthritis deformans is so closely associated with the subject of acidosis that the problem of a review of the literature of the former simply resolves itself into an epitome of the knowledge extant on the latter subject.

In 1880 Hallervorden (1) first observed an increase in the ammonia in urine in cases of diabetes. He concluded that in diabetes there was an overproduction of acids, to neutralize which more ammonia than usual was produced, and thus the abnormal acids were carried out of the body. Furthermore, he regarded the acids as organic in nature.

Walter (2) thought that the acids were inorganic in nature.

Stadelmann (3) succeeded in isolating an acid from the urine of a diabetic. It acted like an organic acid, and he thought that it was identical with crotonic acid.

Minkowski (4) and Külz (5) first fully pointed out the nature of this acid, as they demonstrated that the acid in question was identical with β-oxybutyric acid, and that the croton acid is accordingly not preformed in the urine, but is a secondary product.

This cleared up to a great degree the mystery of diabetic coma, and the view that this coma is an acid intoxication is largely due to the work of Stadelmann, Minkowski, and Magnus-Levy.

Among the various forms of acidosis mentioned in the literature are:

(1) Diabetic acidosis.
(2) Acidosis in children.
(3) Pathological, non-diabetic acidoses of von Noorden.
(4) Acidosis in arthritis deformans.

(1) The literature of diabetic acidosis is very extensive and does not fall within the province of this paper.

(2) There are many conditions in children which are closely associated with an acidosis, conspicuous among them being intestinal disorders of various kinds.

Keller (6) in 1896 observed an increased elimination of ammonia in the urine of children suffering from stomach-intestinal diseases. In some cases the ammonia went as high as 50 per cent.

Bergh (7) is believed to have shown that the increase in ammonia in such conditions was referable to an acidosis, since by giving alkalies he could reduce the elimination of ammonia to a minimum.

Czerny (8) observed that the respiration curves of children who died from chronic wasting diseases had a marked similarity to those of animals poisoned with acids.

The Breslau school pointed out that there was a direct relation between the amount of fat taken in with the diet and the amount of ammonia put out in the urine. Czerny and Keller thought that the fat was the source of the organic acids, and that, in the exhaustion of the infant organism, there arose unknown, abnormal acids which the body in its pathological state was unable to oxidize, as it normally would oxidize acids arising from the fats.

Steinitz (9) considered that the ammonia was used to neutralize the abnormal acids, in order to protect the body alkalies, to avoid the condition of poverty in alaklies, designated by him as alkalopenia. In a case of enterogenous catarrh of the stomach he (10) found a hyperacidity caused by the pyocyaneus bacillus, which possesses the power of breaking down the higher to lower fatty acids.

Rosenfeld (11) noted that a decrease in carbohydrates in the diet causes the appearance of fatty acids and their derivatives in the organism.

An interesting fact in connection with acidosis in children is that the acetone in the breath exceeds that in the excreta by 19 to 60 times.

(3) v. Noorden (13) gives a variety of non-diabetic conditions in which acidosis has been demonstrated.

(*a*) Febrile acetonuria, as in scarlatina, typhoid, pulmonary tuberculosis, etc.

(*b*) Carcinomatous acetonuria by no means rare.

(*c*) Gastro-intestinal acetonuria particularly in acute diseases of stomach and intestines (14).

(*d*) Puerperal eclampsia and the eclampsia of pregnancy.

(*e*) A very uncertain group not yet firmly established; asthma acetonium (15), certain psychoses that Wagner has designated as acetone autointoxication, and certain spasmodic states, described by von Jacksch (16) as epilepsia acetonica. Finally, a disease picture occurring in children, some cases of which have recently been described by Babinsky, characterized by spasms with excretion of acetone. The influence of a diminished diet, especially in carbohydrates, has not been sufficiently considered to place this group on a firm foundation as a clinical entity.

(*f*) Toxic acetonuria, after poisoning with drugs such as antipyrine, morphine, lead, chloroform, narcosis, etc.

(*g*) Starvation and inanition acetonurias.

(4) Very little exists in the literature on the subject of acidosis in arthritis deformans. Helen Baldwin (17) in a study of twenty-one different cases of arthritis deformans found that in all cases of rheumatoid arthritis in which the disease was progressing there was evidence of perverted metabolism, in the nature of an increase in organic acids in the urine. In three cases the stomach contents were examined, and in all there was an absence of free HCl after a test meal. The organic acidity seemed to vary with the intensity of the disease, being greater in severer than in mild cases. Evidences of intestinal putrefaction were found in all the cases in which the disease was active.

Herter (18) found a considerable excess of organic acids in many instances of dilatation of the stomach, and arthritis deformans. Furthermore, he points out that in well-developed intoxications ammonia is the chief base withdrawn from the body, but where the process is very extensive sodium and potassium, and even calcium and magnesium may be removed.

The subject of alkalinity of the body is so intimately connected with the problem of acidosis that it will perhaps be not out of place to consider very briefly the metabolism of calcium, magnesium, and phosphorus.

(1) *Calcium metabolism.*—Calcium oxide is increased in fever, Bencke (19) and Senator (20). Bencke also found the calcium elimination very much increased in chronic wasting diseases, as pthisis and carcinoma.

In diabetes v. Noorden, also Gerhart and Schlessinger, found an increased elimination.

In arterial sclerosis Hirschberg (21) in 1818 found a decreased elimination of calcium.

In arthritis deformans v. Noorden (22) twice found a retention of calcium. Moraczewski (23) found a great loss of calcium in pernicious anæmia.

Calcium is very important for the nervous system. Sabatani showed that the irritability of the brain (cerebellum) is to a large extent dependent on this chemical body.

Magnesium metabolism.—Very little is known of the part played by magnesium in the various problems of metabolism. It is much more easily eliminated by the kidneys than is calcium, and its place of absorption is the small intestine. In starvation (Cetti) the proportion of magnesium to calcium is altered, so that less of the former is gotten rid of by the body.

In arthritis deformans v. Noorden (22) found in two cases a retention of magnesium.

Phosphorus metabolism.—Normally only about 6 to 11 per cent of the phosphorus appears in the stools. In chronic malnutrition the elimination of phosphorus decreases. A diminished elimination is claimed by some authors in fever, and also in nephritis; in the latter case explained by them as due to the lessened permeability of the kidney to potassium salts. An increased elimination of phosphates was found after administration of doses of thyroid gland to a dog, E. Ross (24). Again, W. Scholz (25) has drawn attention to a connection between the function of the thyroid gland and the phosphorus elimination, pointing out that a decrease in its function causes a retention of phosphates, and an increase in its function a corresponding increased breaking down of phosphorous compounds in the body, and consequently an increased output. He draws the analogy of phosphorus standing in the intermediary metabolism to the thyroid gland as does iron to the spleen.

Von Noorden (32) found in three cases of arthritis deformans a retention of phosphorus in each case.

A consideration of the organic phosphates is given later, under division of phosphates.

The patient, Miss B., was a private patient of Dr. Barker's, who presented well-marked signs of the so-called "chronic infectious type" of arthritis deformans. She was assigned to us by him for a metabolic study. The clinical history is given here:

Patient was an unmarried woman, 32 years of age, of frail physique, and weighing on admission only 97 pounds. She complained of swollen and stiff joints.

P. H.—As a young girl patient had had measles, whooping-cough, and chicken-pox, and at this period of life suffered a good deal from catarrh of nose and head. She had not been especially subject to attacks of sore throat. At the age of 15 she had a tumor of the breast removed and there has been no recurrence. The patient has always had a capricious appetite and a tendency to constipation. She began menstruating at the age of 14. Periods have always been painful. During an attack of arthritis the year previous to admission the patient had a cessation of periods for six months.

Habits.—The patient has always led an out-of-door life and lived under the best of hygienic surroundings.

P. I.—The disease began insidiously about four years ago, and has pursued a progressive course until last summer, when the general condition improved somewhat. The patient first noticed that the knuckles began to enlarge gradually and she was unable to get her rings on. They were swollen, but not red or painful. From this, as a beginning, the disease progressed slowly, involving the wrists of both hands, the shoulders, both knees and ankles, giving a typical picture of the polyarthritic type of arthritis deformans chronica. The general nutrition suffered greatly in the course of the disease, the patient loosing 20 pounds.

P. E.—On examination a fairly general glandular enlargement was made out. The clinical findings in the various joints above enumerated showed a typical picture of arthritis deformans chronica, the joints of the hand and wrists being most characteristic. The interossei of the hands were markedly atrophied and the right knee was considerably swollen.

A soft, systolic murmur which was transmitted into the axilla, was made out at the heart apex.

A note by Dr. Rosenheim showed that there was no disease of any of the nasal accessory sinuses. Signs of chronic inflammation in a remnant of the left tonsil were made out distinctly. The patient's right knee was opened by Dr. Sowers and cultures taken remained sterile. Her "opsonic index" to streptococcus, taken by Dr. Meakins, was found to be low.

The patient was put on a known diet, the diet recommended by Otto Folin, the constituents of which are given below. The urine and fæces in 24-hour specimens were collected separately and analyzed for the various constituents given in the tables. Especial care was taken to get the urine in as well preserved a state as possible, and every precaution was taken against analytical errors from bacterial fermentation. The analyses were done, with but few exceptions, everywhere in duplicate, these exceptions being only where the amount of urine, etc., was not sufficient to permit of this procedure.

The period of observation covered five days on the Folin diet, and for three days subsequent to this a few of the constituents of especial interest were followed.

Composition of Folin's Diet.

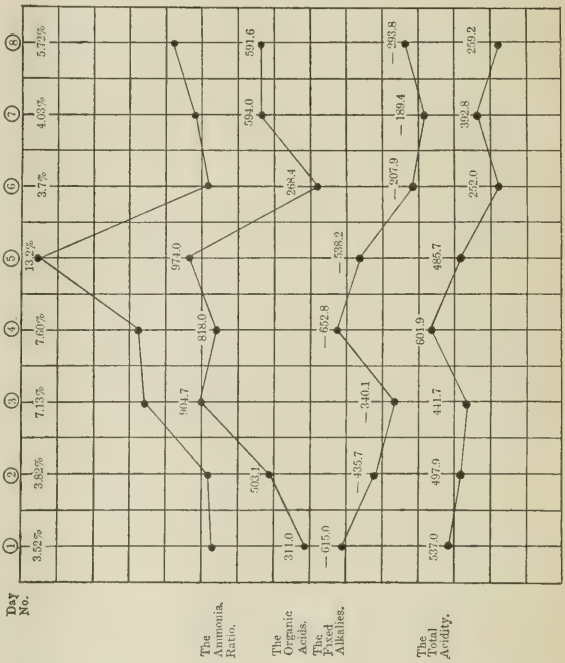
Whole milk	500 cc.
Cream (18 to 25 per cent)	300 cc.
Eggs (white and yolk)	450 gms.
Horlick's malted food	200 gms.
Sugar	20 gms.
Sod. chloride	6 gms.
Water enough to make up	2 litres.
Extra water to drink	900 cc.

This diet was analyzed for the various constituents given in the tables. It was made up in four-litre portions, so that one analysis did for two days nutrition. This diet was found to be a rather hard one for patients to take for any length of time, five or six days being about as long as it could be continued on an average. However, as Folin's valuable studies giving such a variety of urinary data in normal persons are based on this food as a diet, it was deemed advisable to make use of it also in this study of a pathological condition, in order that it might be possible to have a normal standard for comparison. Furthermore, the diet contains ample protein, carbohydrates, and fats, so that the results obtained on such a diet cannot be vitiated by a deficiency in any one of these three important constituents. Proteins, 119 gms., carbohydrates 225 gms., fats 148 gms. During the course of the investigation the patient took exactly the whole amount of food in each 24 hours and exactly the amount of the water allowed, and no drugs were given during this period. The stools were identified by the method of administering charcoal at the beginning and end of the experiment, and were carefully collected, preserved from putrefaction, and dried with addition of hydrochloric acid to prevent loss of ammonia, and powdered.

Folin's diet was calculated for its protein, etc., constituents on the basis of an individual weighing 70 kgms., which corresponds very closely with the value demanded by Voit for an individual of the same weight. As our patient weighed only 35.6 kilo. it will be seen that the diet was very liberal.

Consideration of the Analytical Data.

(1) *The acidity.*—From a consideration of the analytical results, it is quite suggestive that we are dealing in this pathological condition with an acidosis, organic in type, and mild in nature. By consulting the tables it is seen that there is a periodical increase in the organic acids which is most marked on the third, fourth, and fifth days. It will also be seen that coincident with this increase in organic acids and running parallel to it, there is an increase in the ammonia coefficient (i. e. $\frac{\text{ammo.}}{\text{T.N.}}$ ratio), which reaches its highest point 13.2 per cent when the organic acidity is highest—974.0 ccs. $\frac{N}{10}$ NaOH.



In considering the fixed alkalies and earths later, it will be observed that the ammonia is the main factor in combating the acidosis, which in this case is not of such a magnitude as to draw heavily on the reserve force of fixed alkalies and earths that the body needs so essentially for the maintenance of its vital processes. From a perusal of the literature it seems quite apparent that the damage done to the organism in acidosis is not from any inherent property of any special acid, but rather to a diminished alkalescence of the body, produced by the toxic influence of the unknown bodies, characterized by acid properties. So in diabetic coma, which is characterized by an enormous increase in organic acids, it is not any exclusive property of β-oxybutyric acid that gives it such a toxic influence, but rather that it decreases the alkalinity of the blood and diminishes the body's reserve of alkalies, which are indispensable to life.

The inquiry into the causative factor of acidosis has been

directed mainly along the lines of studies of inorganic acids, but the lower fatty and aromatic acids have begun to be studied without as yet very definite results. In this case a test for a number of the simpler acids was made. In none of the urines was there found any trace of acetone, diacetic acid or β-oxybutyric acid. In the aromatic group the test for oxyphenol was positive in every case.

The fixed alkalies.—From a study of the curve representing the elimination of this constituent in the urine it is seen that the fixed alkalies are decreased, varying from $615.0 \frac{N}{10}$ NaOH to 340.7. The elimination is in a general way parallel to that of the organic acids, being at its minimum when the organic acids are largest in amount. It is also roughly parallel to the ammonia ratio, being decreased most when the ammonia ratio is highest. From a review of the proportionate relation in these two elements in the body's chemical mechanism of defense, it would seem that they are both instrumental in combating the acidosis, but by far the greater part is performed by the ammonia.

Phosphates.—A study of the distribution of phosphates is of some interest. In the urinary fraction there is a slight increase in the total and inorganic phosphates on the days when the organic acidity is high, but the most suggestive and interesting finding is in the behavior of the organic phosphates. They are increased, reaching a maximum 0.497 gms. on the day that the organic acidity is highest. The curve of the organic phosphates is roughly parallel to that of the organic acidity.

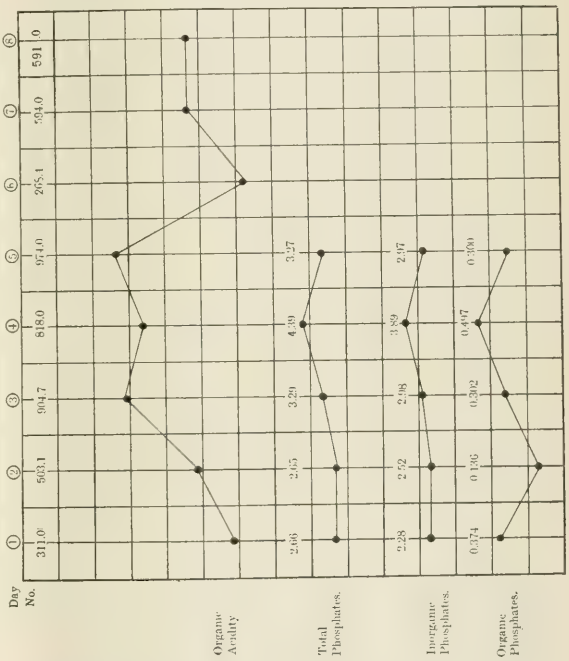
In a normal person the organic phosphates have been found not to exceed .12 gms. in 24 hours (Symmers) and represents from about 2.5 to 4 per cent of the total phosphorus excreted in the urine. In this case of arthritis deformans the amount is considerably larger, varying from 0.136 as a minimum to 0.497 as a maximum, or in percentage of the total phosphorus as high as 14.1 per cent.

The organic phosphates are probably present in the urine as glycero-phosphoric acid, or the more complex compound, lecithin. The latter, on boiling with baryta water yields fatty acids, glycero-phosphoric acid and cholin. So it is not unnatural to suppose that there might be some intimate connection between acidosis and the quantitative elimination of organic phosphates. It would be of great interest to know the cause of the increased elimination of organic phosphates in this case, but as yet little that is positive can be said regarding their appearance in the urine. Symmers (26) has found an increase in this urinary component in lymphatic leukæmia, and nervous diseases of the degenerate type. It has been suggested that the diet might have an influence on the elimination of organic phosphates, but Levy, Mandel, and Oertel (27) have shown that it is practically independent of the diet. So this factor can be apparently safely excluded. It is furthermore unlikely, as Symmers pointed out, that the increase in organic phosphates comes from the bones. Rather it is to be explained as an increase in the organic component of the endogenous phosphorous compounds, or as one of the resultant factors of a lessened power of oxidation on the part of the body.

The table showing the relations discussed above, as well as the curves, showing the relation of the organic acidity to the phosphates are given below.

TABLE I.—ORGANIC PHOSPHORUS.

Day No.	Total P_2O_5 in urine.	Organic P_2O_5 in urine.	Percentage of organic P_2O_5.
I.	2.660	0.374	14.1
II.	2.650	0.136	5.1
III.	3.290	0.302	9.2
IV.	4.390	0.493	11.3
V.	3.270	0.300	9.2
Average.	3.252	0.321	9.8



There was found, as can be seen by consulting the table of balances given, a retention of phosphorus during the entire period of observation, which was least at the height of the organic acidity. This might be expected, as it is well known that there is no mineral constituent which the body holds back as energetically as phosphorus (Albu-Neuberg (28)), and when the phosphorus is increased in the diet, the body does not at once come into phosphorus equilibrium, but retains part of the increased amount. As this is the case, here, where the patient has changed from a mixed diet relatively poor in the salts P., Ca., and Mg. to a diet richer in these components, part of the retention may be simply due to an increased supply; but it may also be advanced that in a disease of the nature of arthritis deformans where there is a waste

of tissues, the body may take a larger proportion of these salts to repair the damage effected by the morbid process.

Calcium and Magnesium.

(1) *Calcium.*—The output in the urine was very constant, varying from 0.88907 gms. to 0.69444 gms., and did not markedly increase with the organic acidity as found by Gerhardt and Schlesinger. It must be remembered, however, that the acidosis in this case is of far less extensive a type than that usually manifested in diabetes.

The amount of calcium in the fæces is largely in excess of that in the urine, varying from 1.05677 to 2.7390 gms. The curves giving the fractional distribution in the urine and fæces as well are given below. From an inspection of these, it is seen that the percentage of calcium in the urine is slightly increased, the figures given by v. Noorden being in the urine from 3.9—20 per cent and in the fæces 71.2 to 96.1 per cent.

In a study of the calcium and magnesium balance in three cases of arthritis deformans v. Noorden and K. Belgard found a retention of calcium (1.28 gms. and 0.75 gms.) and magnesium (.06 gms. and 0.34 gms.) respectively in two cases, and a loss of each in a third. Phosphorus was retained in all three. In this case of arthritis deformans a retention throughout the entire study was observed, varying from 2.10423 gms. on the first day to 0.44135 on the fifth day, or an average of 1.923 gms. Here again as in the case of the phosphorous metabolism, the retention may be due in part to an abnormal richness of the diet in calcium, and in part to conditions caused by the morbid processes of this disease.

Table II.—Calcium as CaO.

Day No.	Calcium in urine.	Calcium in fæces.	Percentage in urine of Calcium output.	Percentage in fæces of Calcium output.
I.	0.88500	1.05677	45.6	54.4
II.	0.72101	2.58650	21.8	78.2
III.	0.88907	2.27390	28.1	71.9
IV.	0.82842	1.72790	32.4	67.6
V.	0.69444	2.11220	24.7	75.3
Average.	0.80359	1.95145	30.5	69.5

(2) *Magnesium.*—The elimination of magnesium in the urine is practically constant, varying from 0.15978 gms. to .10744 gms. It is not increased with the organic acidosis, and evidently does not take a part in the neutralization of the abnormal acids, at least not to any appreciable extent. The percentage in the urine and fæces is about normal, agreeing very closely with the figures given by Bertram and Reuvall, 29-38 per cent in the urine and 67-71 per cent in the fæces. There is a retention of magnesium during the entire period of the study, with the exception of the third day, as shown in the table of balances.

Table III.—Table of MgO.

Day No.	MgO in urine.	MgO in fæces.	Percentage of MgO in urine.	Percentage of MgO in fæces.
I.	0.15978	0.15672	50.5	49.5
II.	0.11390	0.27249	29.5	70.5
III.	0.10744	0.25548	26.9	73.1
IV.	0.11110	0.17357	38.7	61.3
V.	0.11312	0.22910	33.3	66.7
Average.	0.12107	0.21747	35.8	64.2

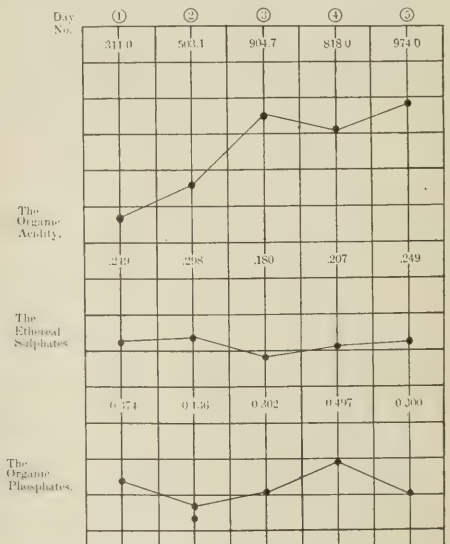
Table IV.—Table of Balances.

Day No.	I.	II.	III.	IV.	V.	Average.	Total.
Total N.....	+0.073	+1.11	+1.39	+0.88	+2.35	+1.16	+5.80
Total P_2O_5.....	+2.339	+2.170	+1.854	+0.850	+1.969	+1.837	+9.182
Total Cl.....	+2.110	+1.131	+0.754	+0.305	−0.048	+0.850	+4.252
CaO.	+3.104	+1.738	+1.639	+1.691	+1.442	+1.923	+1.92
MgO.....	+0.0710	+0.0012	−0.017	+0.082	+0.025	+0.032	+0.162

Uric acid and kreatinin.—The uric acid on this practically purin-free diet is reduced to the so-called endogenous fraction, and is fairly constant, with the exception of the fourth day, when a rise occurs which is coincident with the greatest rise in the organic phosphates, suggesting that on this day there may be taking place an increased destruction of nucleins.

The study of the elimination of kreatinin on a purin-free diet, in the case under our observation, discloses, as did those of Folin, that this factor is practically a constant one and apparently independent of the changes in the total nitrogen. The absolute value of the kreatinin, however, is low in these observations, being about ½-⅓ the amount found by Folin in normal individuals, but as Folin pointed out, this low value can be explained by the fact that our patient weighed only 35.6 kgms., whereas in his observation one patient weighing 87 kgms. gave a kreatinin value of 1.6 gms. and another weighing 87 kgms., a value of 1.15 gms. The findings noted above would appear to be in accord with Folin's contention that on a purin-free diet the chief factor determining the elimination of kreatinin is the weight of the person.

Sulphates.—The inorganic sulphates are slightly increased, varying from 3.6500 gms. to 2.9710 gms. The ratio of the total nitrogen to the sulphates is quite constant, being in the



order of the observations as 1 to 4.7, 1 to 4.0, 1 to 4.1, 1 to 4.2, and 1 to 4.5.

The ethereal sulphates are not increased to any extent, as

compared with those values given by Folin in a normal person on the same diet, varying from 0.1800 to .29838 gms., whereas the latter values do not exceed 20 gms. Their values in the urine are quite constant. The increase is much less marked than that of the organic phosphates, and they show no tendency to vary with the intensity of the organic acidity, as the latter do to a certain extent. A curve to show this relation is here given.

The ratio of the preformed to the aromatic sulphates is not increased above the normal, being in the order of the days of observation as 13.1 to 1, 12.6 to 1, 19.1 to 1, 16.6 to 1, and 11.5 to 1, respectively. The urines were carefully tested in every case for the presence of indol and other products of putrefaction, but with negative results. This was thought necessary, because as H. Baldwin points out, in certain cases of intestinal putrefaction one of the aromatic products may be found in excess while the ethereal sulphates may be normal in amount or vice versa. In this case there is, therefore, no sign of intestinal putrefaction which might be considered to influence the interpretation of the results.

After the study on the Folin diet was concluded the total nitrogen, ammonia, fixed alkalies, total acidity and organic acidity were followed for a period of three days. The patient was on a mixed diet, but was at the same time started on the system of Fletcherizing all the food taken, being required to chew everything to a liquid consistency and being allowed to eat only for 20 minutes. Consequently during this period she received less than the normal amount of food, and the total nitrogen values fell. She also lost some weight in this period.

The organic acidity rose from 268.4 to a value of 594.5 and at the same time the ammonia coefficient also rose from 3.7 per cent to 5.7 per cent. Here again it is suggested that there is developing another periodic increase in organic acids. The fact that the organic acids appear in the urine to be increased periodically, does not of course necessarily mean a similar periodic production in the body, but may be simply a result of improved facilities on the part of the body for their excretion.

It seems suggestive in this case that though the acidosis is mild in degree, and far less extensive than that which occurs in many cases of diabetic coma, and though there is no evidence obtained of a marked disturbance in the alkalies of the body, the long continuation of such a periodic acidosis might well do vital damage to the body. Especially might this be true in cases where the afflicted persons subsist on a relatively insufficient diet, as many no doubt do, particularly with respect to the carbohydrate content. Here the body might be brought into a state of lessened power of oxidation, and then consequently not be able to destroy the abnormal acids formed, necessitating a call on its reserve store of the alkali-maintaining elements of the body.

The question as to how much light the condition of acidosis throws on the etiological problem of arthritis cannot as yet be answered. However, this much may be said that there is some connection between the condition clinically known as arthritis deformans and the occurrence of increased organic acids in the urine of patients suffering from this malady, as is demonstrated by the uniform findings, by H. Baldwin, of an increased organic acidity in 21 cases of arthritis deformans, and this confirmatory case of ours.

Why this disease should show a predilection for the joints and peri-articular structures is not clear, but the physiological knowledge that at these places the circulation is most sluggish may be of some value in attempting to explain this phase of the subject. It might be possible that the acids circulating in the blood would cause a local effect at the joints, proportionately greater than to the rest of the organism.

The fact that in our case no micro-organisms were found in the joint, of course, does not exclude their having been present at one time, and that they may have been responsible either directly or by the action of their toxins for the pathological changes in this disease. Moreover the findings of a chronic focus of inflammation in the tonsils, and the low opsonic index to streptococcus are most suggestive. In this case of arthritis deformans there appears to be a periodic acidosis which may be only a manifestation of a perverted metabolism, or may be more directly considered in the pathological state.

Conclusions.

(1) The metabolic study of this case of arthritis deformans seems clearly to indicate that there is taking place in the organism an acidosis, due to organic acids, and mild in nature.

(2) The acidosis is combated chiefly by the increased ammonia production, and the high ammonia ratio gives an index of the morbid process taking place.

(3) The disturbance in the elements maintaining the alkalinity of the body, the fixed alkalies, calcium, magnesium, and phosphorus is very slight, another indication that the acidosis is mild.

(4) There is an increase in the organic phosphates coincident with the increase in organic acids, the percentage of organic phosphates to the total phosphates reaching as high as 14.1 per cent of the total phosphates.

(5) There is a retention of calcium, magnesium, and phosphates throughout the experiment, which may be partly due to a diet abnormally rich in these elements, and partly to the pathological conditions in the body in this disease.

(6) No evidences of intestinal putrefaction were found in any of the urines, nor was the ratio of the preformed to the aromatic sulphates increased above the normal.

(7) The Folin diet is shown to contain abundant protein, carbohydrates, and fats for the maintenance of the body functions, as the patient gained 2½ pounds on it.

Analytical Methods Used.

Total nitrogen, Kjeldahl.
Ammonia, Folin.
Uric acid, Folin.
Kreatinin, Folin (colorimeter method).

Inorganic sulphates, Folin as SO_3.
Ethereal sulphates, Folin as SO_3.
Inorganic phosphates, Titration by uranium acetate.
Total phosphates, Titration with uranium acetate, after incineration with sodium carbonate.
Calcium, gravimetrically by Salkowski as CaO.
Magnesium, gravimetrically by Salkowski as MgO.
Chlorides in urine by titration according to Volhard.
Chlorides in fæces gravimetrically as Cl_2.
Total acidity, Folin.
Fixed alkalies, Method of Edie and Whitley (Biochemical Journal, 1906).
Organic acidity, Method of Edie and Whitley (Biochemical Journal, 1906).

ANALYTICAL RESULTS.

	Day No.....	I.	II.	III.	IV.	V.	VI.	VII.	VIII.
Food.	Total N..	16.60	16.60	16.74	16.22	16.22			
	Total P_2O_5	5.544	5.544	5.650	5.608	5.608			
	Total Cl..	6.260	6.260	6.200	6.630	6.630			
	Total SO_3	3.760	3.760						
	CaO.....	5.0460	5.0460	4.8220	4.2480	4.2480			
	MgO.....	0.3875	0.3875	0.34675	0.36738	0.36738			
Urine.	Total amount	1770 ccs.	1556 ccs.	1425 ccs.	2315 ccs.	1330 ccs.			
	Total nitrogen	15.36	14.51	14.06	14.77	13.21	8.54	9.90	9.19
	NH_3 nitrogen	0.545	0.585	1.025	1.122	1.748	0.313	0.388	0.526
	Uric acid	0.444	0.286	0.205	0.522	0.212			
	Kreatinin	0.710	0.555	0.600	0.660	0.628			
	Total Cl..	3.130	3.070	2.145	4.370	3.930			
	Total P_2O_5	2.660	2.650	3.290	4.390	3.270			
	Inorg. P_2O_5	2.286	2.524	2.988	3.897	2.970			
	Organic P_2O_5	0.374	0.136	0.302	0.493	0.300			
	Inorg. SO_3	3.230	3.650	3.440	3.450	2.971			
	Ethereal SO_3	0.24898	0.29838	0.1800	0.2076	0.24889			
	MgO.....	0.15978	0.11390	0.10744	0.11110	0.11312			
	CaO.....	0.8850	0.72101	0.88907	0.82842	0.69444			
	Fixed alkalies after incineration in urine.	ccs. $\frac{N}{10}$ 615.0	ccs. $\frac{N}{10}$ 435.0	ccs. $\frac{N}{10}$ 340.1	ccs. $\frac{N}{10}$ 652.8	ccs. $\frac{N}{10}$ 538.2	ccs. $\frac{N}{10}$ 207.9	ccs. $\frac{N}{10}$ 189.4	ccs. $\frac{N}{10}$ 293.8
	Total acidity	ccs. $\frac{N}{10}$ +537.0	ccs. $\frac{N}{10}$ +497.9	ccs. $\frac{N}{10}$ +441.7	ccs. $\frac{N}{10}$ +601.9	ccs. $\frac{N}{10}$ +485.7	ccs. $\frac{N}{10}$ +252.0	ccs. $\frac{N}{10}$ +392.8	ccs. $\frac{N}{10}$ +259.2
	Organic acidity	311.0	503.1	904.7	818.5	974.0	268.4	594.5	591.6
Food.	Total amount	gms. 10.300	gms. 21.900	gms. 34.000	gms. 20.000				
	Total N..	0.511	0.979	1.293	0.566	0.663			
	CaO	1.05677	2.5865	2.27390	1.72790	2.11220			
	MgO.....	0.15672	0.27249	0.25548	0.17357	0.22910			
	Total P_2O_5	0.4448	0.6240	0.5060	0.36770	0.36970			
	Total Cl..	1.0197	2.122	2.301	1.955	2.748			

In conclusion, I wish to express my indebtedness to Dr. C. Voegtlin for the many valuable suggestions and help during the course of this investigation.

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INDEX TO VOLUMES 1-16 OF BULLETIN.

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A METHOD OF PREPARING THE ROMANOWSKY STAIN.

By NORMAN MACL. HARRIS, M. D.

(From the Hull Bacteriological Laboratory of the University of Chicago.)

It it is with hesitancy that I present this brief paper dealing with a topic already so well handled by Wright, Hastings, and MacNeal, especially since there is nothing new to report in regard to staining reactions. My excuse, however, is the fact that in the methods of Wright and Hastings there is a relatively large amount of useful material thrown away; and that the method of MacNeal, to those not masters of technique, imposes a burden on patience, skill, and time, whereas with this method, these drawbacks are to a great extent eliminated and the resulting product is a very serviceable one.

The technique was elaborated through a study of the discussion of the subject by Michaelis, and is as follows: Make up a saturated solution of Grübler's watery yellow eosin in methyl alcohol (Kahlbaum's No. 1) and preserve; then using either "Koch's" "medicinally pure," or "Ehrlich's rectified" methylene blue as made by Grübler, weigh out two grams, powder in a mortar and add nine grams of sodium bicarbonate (c. p.) and mix thoroughly in a dry state, scrape out and place in a beaker of 250 cc. capacity, slowly mix in 25-30 cc. distilled water; cover mouth of beaker with filter paper and heat in an Arnold steam sterilizer for one hour and a quarter. There now remains a blackish fragmented cake and some excess of bicarbonate of soda; remove this black material to a mortar, grind it up and slowly add distilled water, decanting off into a well-stoppered litre bottle, and again add water to 200-250 cc. Any undissolved material is now to be put into the bottle and to the whole is added 10 cc. of a 4 per cent solution of sodium hydrate and then thoroughly shaken. The contents now assume a deep maroon color.

The next step is to extract with chloroform (commercial). For this purpose it is best to have at hand an extracting funnel[1] of 500 cc. capacity, though one of 250 cc. will do, and a couple of 500 cc. beakers or other suitable vessels, and a 15 cm. porcelain evaporating dish. To the contents of the liter bottle add at once 150 cc. of chloroform and shake moderately for 2-3 minutes, pour into the separating funnel and draw off the now deeply-colored chloroform into the beaker. The color of the watery solution should then be a pale blue, showing that extraction is practically complete; if still deep blue, add 3 cc. of the sodium hydrate solution, shake and further extract with chloroform.

Not infrequently it will be found that a portion of the chloroform becomes emulsified and will not separate. It must then be poured back into the liter bottle with the watery solution, 2-3 cc. sodium hydrate added, together with 50 cc. of fresh chloroform, and again shaken. Some emulsification is always present and a loss of 10 per cent of the chloroform usually results; however, by the addition of the 50 cc. of fresh chloroform, any resultant emulsified chloroform will contain so little extractive as to constitute no real loss.

It is now well to run the whole of the separated chloroform solution through the funnel once more to be sure to remove any of the original watery solution or emulsified chloroform that might have inadvertently gotten in. Then pour into the porcelain dish about 50 cc. at a time and evaporate completely over a water bath. As evaporation is nearing completion, often the sticky mass bubbles too actively and may spatter; this may be avoided by letting the water simmer gently for a while. Ultimately, the mass becomes dry, hard, of a deep violet-blue and covered with a brilliant yellow luster. This mass is made up largely of methylene violet, variable amounts of methylene azure and other substances.

Now scrape off as much as possible with a knife and put this into a glass-stoppered bottle of about 200 cc. capacity; add gradually, while stirring with a glass rod, to what remains of the extract in the dish some 30 cc. methyl alcohol (Kahlbaum's No. 1), and pour off into the bottle, filling the same three-quarters full with methyl alcohol. This constitutes the saturated stock solution of crude methylene violet and azure.

To make the staining fluid, take of the stock solution 66 cc., of methyl alcohol 33 cc., of the saturated methyl alcohol solution of "yellowy watery" eosin 1-1.5 cc. Bottle it and add from 0.05-0.15 gram of methylene blue.

The staining is carried out as in Wright's method, the coverslip or slide being not too scantily covered with the dye, which acts for one minute alone; then to this is added drop by drop a quantity of water equal to the bulk of the dye, after which the slide is allowed to stand for five minutes. Wash for 1-2 minutes in running water. This method stains excellently cells, and also brilliantly both the chromatin and protoplasm of trypanosomes (Tr. lewisi), Entamoebae histolyticae, and malarial parasites. If dysenteric stools are to be stained, the dye should be left in contact two minutes before mixing with water. To stain Treponema pallidium (Spiroch, pallida), carry out the staining as for blood films, but extend the time to ten minutes; the treponemata are readily found and well-stained of a pink-violet color. There is little or no precipitation if one is careful not to add too much water.

I have used the stain for a year past and have found it satisfactory. My hearty thanks are extended to Doctors Boggs, Cohoe, and Geraghty, of the staff of the Johns Hopkins Hospital, for the supply from time to time of blood films and other materials for study, and to Drs. J. H. Wright, T. W. Hastings, and W. J. MacNeal for samples of their stains used as comparative standards.

[1] In the absence of a separating funnel the litre bottle may be converted into one by fitting to it a rubber cork through which are passed two glass tubes, one reaching to the bottom of the bottle, the other flush with the cork. By fitting to the former tube rubber-tubing and a pinch-cock, the chloroform solution may be completely drawn off on inverting the bottle.

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THE OPERATIVE TREATMENT OF SUBDELTOID BURSITIS.

By W. S. Baer, M. D.

The part which injuries and inflammation of the subdeltoid bursa play in the restriction of motions at the shoulder joint has been brought strongly to our attention within the past few years. Formerly it was supposed that most if not all of the causes of partial or complete anklylosis of the shoulder were to be found within the joint. Roustan[1] in 1880 in a pathological study of periarthritis and bursitis of the shoulder divided his cases into acute, subacute, chronic, serous, purulent and fibrous bursitis. Jarjarvay,[2] in examining the cadavers of laboring men, called attention to the distinct thickening of the subdeltoid bursa and pointed out the traumatic factor in their etiology. Finney,[3] in the early days of this hospital, gave us a clinical picture of the affection and demonstrated a painful spot just below the coracoid process. It has remained for Codman,[4] however, in a very graphic paper to give us a complete anatomical demonstration as to the manner in which the inflamed subdeltoid bursa prohibits the full motion of the head of the humerus in the glenoid cavity.

Anatomy.—The subdeltoid bursa is about the size of a silver half-dollar and is composed of either one or two parts. When divided in two, the individual parts are sometimes spoken of respectively as the subacromial bursa and the subdeltoid bursa. The subdeltoid bursa, as its name indicates, occupies a very exposed position directly beneath the deltoid muscle. Its inferior surface is closely adherent to the joint capsule. It thus separates the deltoid muscle from the humerus and from the tendons of the long head of the biceps and the supraspinatus muscle which lie beneath the capsule. The walls of the bursa are very thin and it has the usual serous lining. As the arm hangs naturally at the side of the chest a small portion of the bursa lies beneath the acromion process, and this portion is spanned by the coracoid-acromial ligament. As one abducts the arm the bursa passes beneath this ligament. If you recall the relation of the coracoid and the acromion processes you will remember that the former lies on a much lower plane than the latter. So it is that the coracoid-acromial ligament prevents the swollen bursa from passing beneath it, and thus prevents the abduction of the arm to any degree. Together with Dr. Fayerweather I have injected the subdeltoid bursa with wax, the cadaver having been first immersed in hot solutions to allow freedom of motion. The wax in the bursa is then allowed to harden. Various motions of the shoulder joint were then attempted. It will be seen, as in the accompanying drawing, that if the bursa is slightly swollen all abduction, except the first ten degrees, will be prevented by the coracoid-acromial ligament. This ligament acts as an absolute hindrance to the further progress of the bursa beneath it. Now as we must have more abduction than this before we can internally rotate the arm to a sufficient degree to carry the hand behind the body it is easily seen why this is one of the characteristic restrictions in cases suffering from subdeltoid bursitis.

Etiology.—The causes of this affection are varied. When we recognize that the subdeltoid bursa is lined with a serous coat we must further recognize that it may be subject to all changes which are usually found in serous sacs, namely, serous effusions, inflammatory conditions from trauma and strain, infectious processes due to the gonococcus, tubercle bacillus, rheumatoid arthritis, etc. The main etiological factor, as shown by our cases, is trauma—trauma due to direct violence, trauma due to occupations which put the bursa under constant strain.

Pathology.—There are different pathological changes according as there are different etiological factors. In mild cases the walls of the bursa are perfectly normal, but there is an extra amount of fluid within the sac. In others the walls are slightly thickened. The lining membrane is hyperæmic and swollen, and the surfaces of the bursa are partially adherent by bands of fibrin. Some show complete obliteration of the bursal cavity, the walls being densely adherent, and at times more than 1 cm. in thickness, due to the new formation of scar tissue. If the process is a tuberculous one the cavity may be filled with a dense cheesy material.

Pain.—In the acute cases there is intense pain, but after the first few days of the disease pain is only present when an attempt is made to abduct the arm. At times the pain is worse at night owing to the inability of the patient to move the arm into any comfortable position. On pressure pain is generally elicited directly at the site of the bursa, but often it is referred along the bicipital groove or along the anterior aspect of the arm.

Swelling.—At times and especially in acute cases and in chronic cases where there is a marked thickening of the bursa a distinct swelling may be made out on the anterior aspect of the humerus just below the coracoid-acromial ligament.

Atrophy of muscles.—In long persistent cases there is an appreciable atrophy of the supraspinatus and infraspinatus muscles, and also at times of the biceps. These muscles, however, show a normal reaction to faradic and galvanic stimulation.

Restriction of motion.—This is the main physical sign of the disease and the one for which the patient seeks relief. In the older cases one can abduct the arm 10 to 15 degrees, but can go no further. The anterior motion of the arm is free, and the posterior motion is generally fair, but internal rotation is completely lost so that the patient cannot place the hand behind the body. Occasionally when the bursa is but moderately thickened, if one rotates the humerus outward so that the bursa is as far removed as possible from the coracoid

[1] Roustan: Montpellier méd., 1880, pp. 44 and 45.

[2] Jarjarvay: quoted by Putnam, Boston Med. and Surg. Jour., November 30, 1882.

[3] Finney: Johns Hopkins Hospital Bulletin, 1894, p. 83.

[4] Codman: Boston Med. and Surg. Jour., Vol. CLIV, p. 613, 1906.

end of the coracoid-acromial ligament, the arm can then be abducted to its full extent. As the bursa passes beneath this ligament one can feel a decided click just as one feels on the reduction of the congenital dislocation of the hip when the head of the femur goes over the posterior rim of the acetabular cavity.

Radiograph.—As a rule the radiographs in these cases are negative, and in this they allow us to make a differential diagnosis from cases of fracture of the greater tuberosity of the humerus which clinically are rather hard to differentiate. Occasionally, however, when the bursa is replaced by dense scar tissue there is a shadow to be seen in the radiographs at the point of the subdeltoid bursa.

Treatment.—What then shall be the mode of treatment of these cases? Let me here give an account of four cases which we have recently operated upon before discussing the question further.

CASE I.—G. M., male; age, 38 years; occupation, label cutter in a lithographic firm; admission, October 18, 1905. Complains of a painful shoulder and loss of motion in it.

Family history.—Negative.

Previous history.—Negative; denies lues and "tripper."

Present illness.—The patient's occupation is such that his right arm is constantly in action as he uses it with his machine in cutting labels. Eighteen months ago he first noticed pain in his shoulder. At no time has there been any redness or local heat, no evidence of any acute inflammation. The inability to use his arm has grown so bad that three months ago he was compelled to stop his work. His sleep is very much disturbed owing to his inability to get into a comfortable position.

Physical examination.—Very well-nourished man. Right arm hangs at his side. There is no particular atrophy of the supraspinatus or infraspinatus muscles, but there is a slight atrophy of the biceps. There is a slight fullness just below and to the outer side of the coracoid process. At this point it is somewhat tender and there is pain referred along the bicipital groove. As long as the arm hangs at the side there is no pain either on the internal or external rotation. The arm can only be abducted to 15 degrees and the patient is absolutely unable to put the arm behind his back. The radiograph shows the joint to be normal, but there is a slight blur near the greater tuberosity of the humerus, the site of the subdeltoid bursa.

October, 1905, under an anæsthetic I made an incision 4 cm. long midway between the coracoid and acromial processes running longitudinally to the humerus. The fibers of the deltoid muscle were separated and the subdeltoid bursa exposed. It was found to be somewhat thickened, the walls were injected and there were marked fibrous adhesions between the surfaces. The bursa was entirely excised. Cultures were taken and proved to be negative. The examination of the pathological specimen showed newly-formed fibrous tissue containing a great number of small blood vessels. In order to be sure that all the disability was due to the bursa an incision was made into the capsule and the joint explored. It was found to be entirely normal. The capsule was sewn with fine black silk. The muscle fibers were brought together with silk and the skin with subcutaneous silver wire. The arm was then put up in a splint in the position of abduction to 120 degrees and kept there for a week. This position was extremely trying. At the end of the week the splint was removed and the patient was allowed to go without any other support. Fourteen days after the operation he had a voluntary motion of 120 degrees of abduction, perfect inward and outward rotation, and could put his hand behind his back with perfect ease. He returned to his work on his fourteenth day. He reports to-night, twenty-one months after the operation. He has worked continuously at his trade ever since that time. The motion at the shoulder joint is perfect in all directions.

CASE II.—H. L., white; age, 23 years; admitted, January 21, 1907; occupation, plasterer. Complains of lameness in his left shoulder.

Family history.—One maternal aunt died of pulmonary tuberculosis.

Previous history.—Negative; denies venereal infection.

Present illness.—Six months ago while at work he noticed a pain in the left shoulder, which gradually increased to such an extent that he was obliged to stop his work, and he has been unable to do anything for the past five months. He cannot raise his arm without intense pain, which is referred along the anterior surface of the arm. Whenever he attempts to move the arm at night it is so painful that it immediately awakens him. He thinks the soreness is greater in damp weather.

Physical examination.—If the left arm is abducted 10 degrees a decided click is felt and the arm refuses to go any further in that direction. There is considerable amount of pain referred in the region of the bursa and down the front of the humerus. There is a decided fullness over the bursal region. There is practically no atrophy of any muscle.

Operation.—Under anæsthesia on January 25, 1907, I made an incision through the deltoid muscle as in the last case. The bursa was found to be much swollen almost 1 cm. in thickness. The walls were closely adherent and it was apparently one mass of scar tissue. Before removing the bursa the arm was abducted and the bursal sac impinged on the coracoid-acromial ligament and further abduction was prevented. The bursa was removed in its entirety and then full abduction was allowed. The muscle was closed with interrupted silk and the skin with subcutaneous silver. Owing to the discomfort caused by a splint, which would keep the arm at right angles as in the previous case, the arm was allowed to hang at the side and put in a Velpeau bandage. February 3, nine days after the operation the subcutaneous stitch was removed and the patient could bring his arm to a right angle. One week later, sixteen days after the operation, the patient could voluntarily bring his arm to the full amount of abduction, and had perfect use of it in rotation inward and outward. He went to work on his seventeenth day, having previously been out of work for five months. To-night, two and a half months after his operation, you see the motion is absolutely normal and has been so since his eighteenth or twentieth day. A culture taken from the bursa at the time of the operation proved sterile. The pathological report shows a mass of hard fibrous inflammatory tissue with much round cell infiltration.

CASE III.—A. G., white; age, 39 years; admission, April 22, 1906. Complains of inability to use her left arm.

Family history.—Negative.

Previous history.—Negative.

Present illness.—Fell on the ice and struck her shoulder three months ago. Since that time she has been unable to raise her arm at all and it has been impossible for her to get her hand behind her.

Complains of considerable pain along the bicipital region on moving the arm to the slightest degree. Her sleep has been greatly interfered with owing to inability to assume a comfortable position.

Physical examination.—Shows atrophy of the supraspinatus and infraspinatus muscles. She cannot raise her arm (that is abduct it) more than 10 degrees, and even this is very painful. Rotation inward and outward is materially restricted, though not to the same extent as abduction. Practically no swelling of the shoulder could be made out. The pain is referred down the front of the

arm. The radiograph is absolutely negative. May 1, 1907, the patient was anæsthetized and operated upon as in the first case. The bursa was found to be very thick, approximately 1 cm., and the walls densely adherent at the lower end of the bursa. At the upper portion of the bursa two walls were distinct, but they were much reddened and hypertrophied. The bursa was removed, and the closures were the same as before. The arm was put up in a Velpeau bandage. Two weeks after the operation the voluntary power of abduction was 90 degrees, and the rotation outward and inward was normal. At the end of the three weeks all motions were normal.

Case IV.—A. K., colored; age 46 years; admitted February 25, 1907; occupation, laborer. Complains of inability to use his right arm.

Family history.—Negative.

Previous history.—Negative.

Present illness.—Two months ago he fell twenty feet from a scaffold and struck on his right shoulder. The shoulder became swollen, but it did not keep him from his work. Three days later the swelling and pain had somewhat subsided, but he was unable to work owing to the inability to use his arm.

Physical examination.—Showed a slight swelling over the region of the subdeltoid bursa. There was no atrophy of the muscles. The pain was referred down the front of the arm and beneath the acromial process. The arm could be abducted to 15 degrees but could not be placed behind him.

Operation.—The patient entered the service of Dr. Halsted and I operated, as in the preceding cases, on February 26, 1907. The bursal walls were thickened and adherent one to the other so that the cavity was entirely obliterated. There had been a slight comminuted fracture of the greater tuberosity of the humerus, and the capsule and bursa were both adherent at that point. The bursa was removed and the capsule freed from the tuberosity. The wound was sewn as in the previous case and the arm put up in the Velpeau bandage. All dressings were removed on the eleventh day. On the fourteenth day the motion was greatly improved, abduction being allowed to 40 degrees, and internal rotation was almost perfect. To-day, seven weeks after the operation, he can abduct his arm to the right angle without pain notwithstanding the fracture of the tuberosity and the tacking down of the capsule.

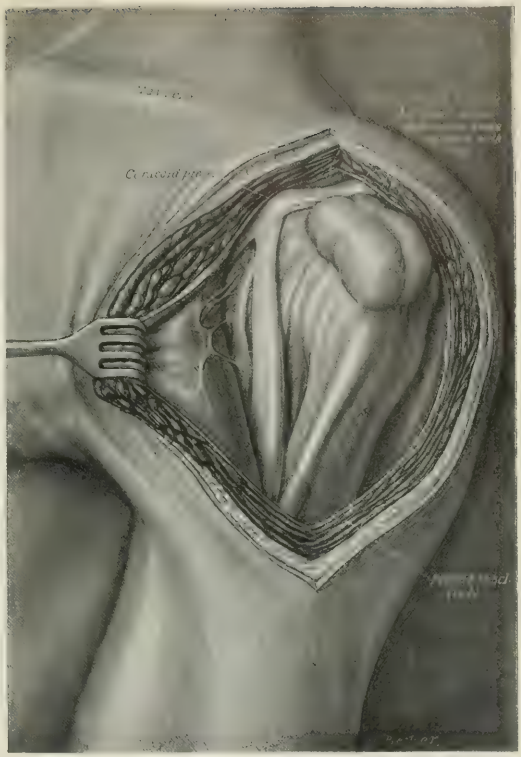
In the acute cases the treatment is obvious. Reduce the swelling of the bursa and relieve the pain. This may be done by the application of ice bags to the shoulder, or by the use of counter-irritants as the Paquelin cautery or hot air. If the inflammation is of rheumatic origin, the salicylates or aspirin prove valuable. Besides medication the arm should be put at rest to prevent traumatism of the bursa.

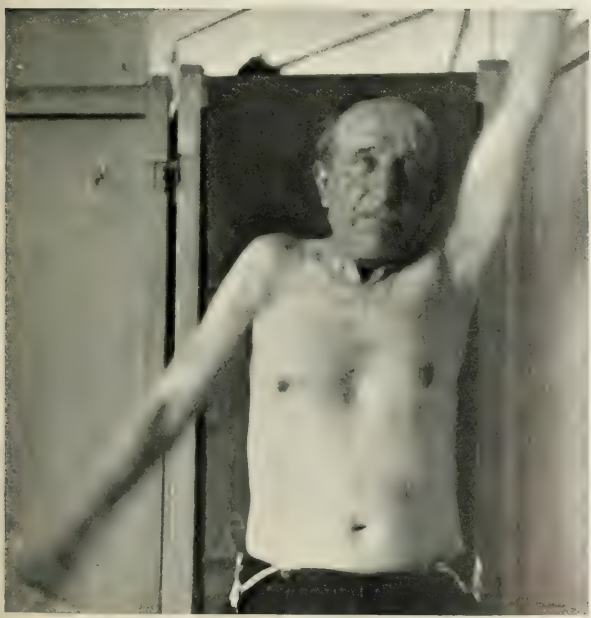
It is the more chronic class of cases which claims our especial attention in this paper—those cases which have resisted the treatment as indicated above, and have persisted for some time. I am sure we are all familiar with the clinical picture as shown in the cases just reported, and of the long and tediously painful course which they run, a course which often wears out both patient and doctor before they are relieved. Putnam[5] in 1882 recommended that the adhesions about the shoulder joint should be broken up by repeated manipulations under anæsthesia, and that passive motions and massage be given continuously. This we have found to be very trying to the patient, and indeed it takes a patient with great stability to submit to repeated anæsthetizations and continuous passive motions. In fact, many a patient has been brought to the verge of a nervous breakdown, if not actually pushed over the brink, by the constant pain which persistent passive motions necessitate. Codman's method of treatment is to break up the adhesions by forcible manipulations under anæsthesia, and to put the arm up in a splint which retains it in abduction of at least a right angle, and at the same time in rotation outward. The splint is left on for 24 hours continuously, and then for a week or more, daily taking the arm down for a brief respite. The idea is that this position of abduction and rotation will bring the raw surfaces opposite healthy ones. I think this method of treatment has its drawbacks. In the first place serious damage has been done by an attempt to break down the adhesions in this manner. Dislocations of the head of the humerus have occurred, as well as thrombosis of the axillary vessels. In the second place the position of marked abduction and rotation outward is tiresome in the extreme, if persisted in for any length of time. Further, adhesions will very often reform necessitating further manipulations and certain continuous passive motions for quite a period of time. Finally, there are certain cases where the bursa has been transformed into fibrous tissue of such a thickness that it would be absolutely impossible to pass it under the coracoid-acromial ligament. The method which I have outlined in this paper is the complete excision of the bursa. I do not believe with Codman "this bursa is indispensable in abduction and rotation of the humerus."

An incision of small extent should be made parallel to the long axis of the humerus midway between the coracoid and acromial processes. The fibers of the deltoid should be separated, and we come down on the subdeltoid bursa. This should be dissected out and removed in its entirety. If the walls of the bursa are at all thickened this is easily done, but if the walls are normal the sac is so thin that one is liable to overlook it. After the sac has been excised the arm should be put through all its motions, which one can then do, without fear of untoward results. The biceps muscle is brought together with fine black silk and the skin is sewn with subcutaneous silver. The arm should then be put up in a Velpeau bandage and dressed on the seventh day. The arm is then entirely freed and the patient allowed to use it at will. In reviewing our cases the advantages which the operative treatment affords are as follows: There is no fear of damage from tearing the adhesions, or rupturing the vessels, for all adhesions are removed in situ before the manipulations are commenced. The bursal walls cannot re-adhere, for they have been removed. The position at which the arm is placed at the side of the patient is most comfortable. The patient is saved a long course of passive motions and massage, which is very trying, and can return to work with full motion and painless use of the arm in from two to three weeks.

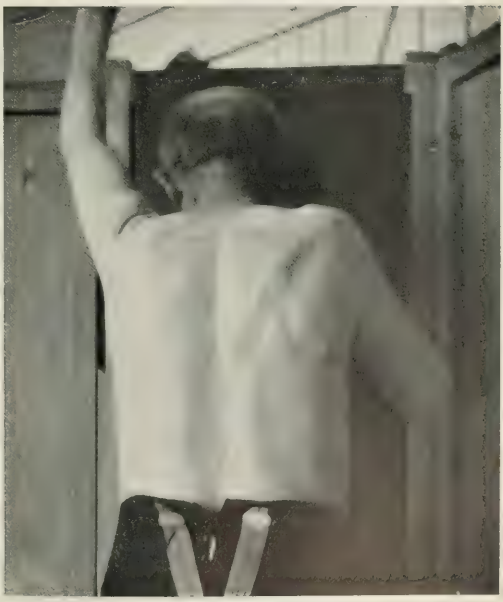
[5] Putnam: Boston Med. and Surg. Jour., November, 1882, p. 536.

CASE I.—Possible abduction 14 days after operation.





Both arms are abducted to their full extent.



Both arms are abducted to their full extent.

The arrow indicates position of bursa.

Fracture of greater tuberosity of humerus.

NOTES ON NEW BOOKS.

Modern Medicine. A System edited by WILLIAM OSLER, M. D., assisted by THOMAS MCCRAE, M. D. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

It is about twenty years since the appearance of the System of Medicine edited by the late Dr. Pepper. Systems are like pandemics, they appear only at long intervals. Some would say that they might be dispensed with; that we could get along very well with the endemic text-book or monograph. Of the great value of monographs there is no question but the profession as a whole pays little attention to them. The aim in a System of Medicine should be to have a series of articles which are to some extent on the order of monographs so that the practitioner can refer to a scholarly statement of the subject without the introduction of too much controversial or doubtful matter. Some men say that an article in a System is buried. As a rule it is, if it deserves burial. But good articles are constantly referred to and serve as a standard source of reference. Take for instance the article by W. H. Welch on Ulcer and Cancer of the Stomach in Pepper's System. No writer on these subjects since then can afford to neglect them. We know how often the teacher refers his students to various articles in Allbutt's System.

In this System Dr. Osler has drawn largely upon the young men in the profession; he has chosen his contributors rather from those who are breasting the hill than from those who have reached the summit or are looking toward the sunset. The general order followed in the volumes rather suggests that of some of the more recent French Systems. In arrangement and form it must be said that thus far the French have surpassed Germans, English, and Americans in the preparation of Systems of Medicine.

This volume opens with a short article on "The Evolution of Internal Medicine" by Dr. Osler. In this brief survey he notes the general forces which have influenced the development of our art from early times to the present. With this the aims of the present work are described and the hopes for the future. In the majority of his articles some references are given which demand search from the average reader. We wonder to how many the word *Nehushtan*[1] conveys any meaning.

Dr. Adami of Montreal writes on "Inheritance and Disease." As might be expected, he deals with a difficult subject in a clear and scholarly manner. Inaccurate ideas as to heredity and inheritance are common, which such an article should help to set right. Dr. Adami devotes special attention to a physico-chemical theory of inheritance under which emphasis is placed on conditions which affect the tissues of the parent and also the germ-cells.

The diseases caused by physical agents, light, heat, electricity, etc., are dealt with by Dr. Gordon. The tremendous increase in the use of electricity and the amount of work done with the X-rays renders these sections important. Under the subject of light and heat, writers do not seem to have arrived at a very clear separation of the various forms of disease. Dr. Edsall has given us in the section on diseases caused by chemical agents a most satisfactory discussion of the subject. He draws attention to the fact that in this country there has been no official effort directed toward the study or control of dangerous trades. Throughout his articles there are references to the regulations of other countries which suggest the importance of similar legislation here. The diseases caused by alcohol, opium, and cocaine are discussed by Dr. Alex. Lambert of New York. His work in the Bellevue Hospital has given him a wide experience and the lesions should be well-marked when we read that "not infrequently, at least among the Bellevue Hospital patients, a pint (of cheap whisky) is reckoned as a single drink." He discusses the various doubtful points as to the effect of alcohol in a fair spirit and without the bias evident in so many articles. Special attention is drawn to the symptom-complex of "wet brain." The notice given to opium smoking suggests a greater prevalence in one or two large cities than in the country generally.

Dr. Novy discusses Food Poisons and it is interesting to note how little relative importance is given to ptomaines compared with bacterial infections. The greater part of the article deals with bacterial poisons. Dr. Noguchi takes the subject of Snake Venoms on which he has done so much work.

The subject of Auto-intoxications is taken by Dr. A. E. Taylor. It is not possible to review this article in detail, but it is to be hoped that it may help to clear away many of the erroneous views regarding this subject. Many of the profession have accepted statements for which there was no basis and have made the term "auto-intoxication" a convenient diagnosis for obscure conditions and sometimes for conditions not so obscure. The gastro-intestinal auto-intoxications are taken up first and it is interesting to see how little accurate basis there is for the many views held regarding their importance. Abnormalities in oxidation, retention intoxications, and those in relation to salts, acids, and alkalies are discussed. In the second chapter on this subject the auto-intoxications associated with the metabolism of the various groups of foods are gone over. In some senses, gout and diabetes may be regarded as coming under the heading of auto-intoxications. Altogether, Dr. Taylor has written a most satisfactory article on a difficult subject.

Dr. J. H. Wright contributes the section on Actinomycosis and Nocardiosis, which he is well fitted to handle from his thorough work on them. Introductory to the Diseases caused by Protozoa are sections on the Protozoa by G. W. Calkins and on mosquitoes by L. O. Howard; each is an authority on his subject. The article on Malarial Fevers is by Surgeon C. F. Craig of the U. S. Army. In the discussion of the æstivo-autumnal parasite he takes the view that there are two varieties, the quotidian and tertian. This follows the opinion of many Italian observers, which, however, is not held by many in this country. That subject of much discussion, Black-water Fever, is discussed by J. W. W. Stephens of the Liverpool School of Tropical Medicine. He argues strongly for the influence of malarial infection and considers Black-water Fever not as a disease *per se*, but a condition of the blood *produced only by malaria* in which quinine, other drugs, cold, etc., may produce a sudden destruction of red cells. Col. David Bruce of the British Army writes on Trypanosomiasis, on which he has done so much work. Dr. R. P. Strong of Manila has the section Amœbic Dysentery and contributes an article drawn from experience both in this country and the Philippines. He directs attention to the association of intestinal hæmorrhage and liver abscess in amœbic dystentery.

The section on Animal Parasites is written by Dr. C. W. Stiles, who has made a splendid article without too much detail and yet very complete. Until now we have lacked such a comprehensive discussion which was readily available and this impresses us as the best article in English on this subject and should be of great value to the general practitioner who has not access to the more elaborate works.

The section on metabolism opens with an elaborate discussion on Nutrition by Professors Chittenden and Mendel of Yale. The work of the Yale School on this subject is well known and they have given a comprehensive article in which the general considerations are first discussed and then the various modifications of metabolism under changing conditions. The changes which the various foods undergo and especially the importance of inter-

[1] To save the reader's time, he is referred to 2 Kings xviii, 4.

mediary metabolism are fully taken up. With this the question of the disorders of metabolism is closely associated. As is well known, Professor Chittenden holds strongly that for many persons "the nutritive demands are certainly more than satisfied by the customary dietaries." Whether one is willing to go the length to which he does, there can be no question of the importance of the matter and the necessity of careful study of this subject. The article closes with the discussion of the composition of the various foods in their relation to nutrition and the constituents of various systems of diet.

The articles on Diabetes Mellitus and Insipidus, and Gout are by Dr. T. B. Futcher. These are most thorough and satisfactory, and may be pointed to as examples of what System articles should be. Dealing with diseases characterized by complicated chemical disturbances, the information on these is set forth with such clearness and detail that no one can fail to understand. The clinical side is well gone over and fully considered. The discussion of the treatment of these diseases is very rational, that on Diabetes Mellitus especially so. In Diabetes Insipidus it is interesting to note the great importance placed on syphilis as an etiological factor. The articles by Taylor, Chittenden and Mendel, and Futcher all deal to some extent with the questions of carbohydrate and protein metabolism. It is interesting to compare these and see the points of view which result from the different aspects which each considers.

Dr. J. M. Anders deals with obesity and gives full discussion to the modes of treatment. Dr. Still of London writes on Rickets both in early life and in its late manifestations. Dr. Hutchinson of London contributes the section on Scurvy. Both of these are comprehensive articles.

Altogether this volume is most satisfactory and sets a high level for the succeeding ones to maintain. There is so much which might be commented on that it is difficult to choose. Dr. Osler has been fortunate in many instances in having contributors who have specially identified themselves with the subjects which they discuss. As he says in his Introduction, it is not always easy for men who are saturated with their subject to keep within limits and remember the practical character of the men who read, yet we think that the contributors have kept this in mind and succeeded.

The publishers have done their work well. The page is attractive, the type is clear, the illustrations are well done, and the book lies open well at any page, a quality as admirable as rare.

Diseases of the Lungs. By Robert H. Babcock, A. M., M. D. First Edition. (*New York: D. Appleton & Co., 1907.*)

This is by the author of the splendid work on the "Diseases of the Heart and the Arterial System" (Appleton, 1903) and is intended to complete the work on the "Chest." As the author explains in his preface, the object of the book is to present "these as well as other subjects in a manner that will render them available to the student and practitioner of medicine, since the book is not intended for the experienced internist, whose knowledge may surpass that of the writer. There is nothing novel in method, and no wearisome discussion of unfounded theories. The aim has been to be practical and hence ætiology, diagnosis, and treatment have received especially full consideration."

We may say that the author fully lives up to his words throughout the whole book, which is to be specially commended. The work is of about 800 pages, being divided into three parts, the first is devoted to the "Bronchi," each chapter covering its separate field most thoroughly and especially in regard to treatment. The author uses the term "Plastic Bronchitis" in place of the older one "Fibrinous" on the assumption that we are not certain in all cases that the casts are composed of fibrin.

The second section is divided into the diseases of the "Lungs" proper and covers about 550 pages. The subject of Pneumonia (lobar) is considered under the name of Acute Fibrinous Pneumonia, which the author chooses instead of Lobar, as being more correct and at present in wide use among the Germans. Fibrinous Pneumonia was the term chosen by Virchow, on account of the richness of the exudate in fibrin. In speaking of the designation "lobar" the author says: "It is now known that the local process may have a lobular as well as a lobar distribution, and, therefore, this term is not scientifically accurate." It has the sanction of usage, however, because agreeing with the facts in most cases, and is the name most commonly given to the diseases in this country. As stated, he says he will use the terms lobar, croupous, and fibrinous interchangeably in the article.

The whole article on Pneumonia is splendidly written, being extremely clearcut and logical; the chapter on treatment is especially timely and the danger of overdrugging is forcibly brought out, and fresh air is given its most important place in the modern management of patients. The author cites many cases from his hospital and private practice, which illustrate many points and are interesting, but in some instances a little too lengthy.

The section on the lung disorders is thoroughly up to date and complete, that on Pulmonary Tuberculosis in particular; in the ætiology of this disease, the author has an especially valuable chapter and touches well on the conditions of life and environment. The story of the poor, and of tenement life in the great cities is appealingly and forcibly told. The symptomatology and diagnosis are well brought out, the prevention and treatment exhaustively considered, and the educational side of the question, with the relation of the state and municipal control is well accentuated. The sanatorium, dietetic, and climatic treatment is most completely detailed, and "drug therapy" considered, as the author says, "not for the purpose of its indorsement, but to condemn it in the most emphatic terms possible."

In closing the section on treatment the author gives good briéf summaries of Tuberculin and its actions, the different serums, and the production of artificial immunity.

The general diseases of the lungs are all considered at some length and most thoroughly, and in the last section the inflammations and diseases of the Pleura are treated of in about 80 pages most carefully.

In the first edition of any work numerous typographical errors are bound to creep in; among these we may mention the following:

In the table of contents, p. x, the line under treatment of pneumonia should read *with a physiological salt solution.*

On p. xii heading of chapter xxviii, should read *Pneumonic.*

In the text, p. 210, bottom line, the word *râles* is left out.

On p. 618 the 12th line from bottom *antitoxic* should be put in place of toxic.

On p. 77 fig. 8 has no reference to it in the text.

On p. 443, fig. 54, *upper lobe* should read *lower lobe.*

As regards the illustrations they are as a rule well reproduced and represent clearly what the author desires to show; the photographs are good, but the plates are in some instances a little too diagrammatic.

The book as a whole is very well gotten up by the publishers and can certainly be commended highly "to the practitioners and students of medicine," and will serve as a splendid companion volume to the author's work on the Heart and Arterial System.

J. A. Chatard.

Tuberculosis, as a Disease of the Masses and How to Combat It. By S. A. Knopf, M. D. Fourth Edition. (*New York: Published by Fred. P. Flori.*)

A brief but clear and satisfactory supplement on Home and

School Hygiene is the only important addition to the last edition of this "Prize Essay." "The short historical review of the anti-tuberculosis movement in the United States from its beginning to the present day," which has also been inserted by the author, seems to the reviewer out of place in this pamphlet. There is nothing new to be said about the original essay whose value is measured by its world-wide fame, and the call for a fresh appearance. R. N.

A Treatise on Surgery. By GEORGE RYERSON FOWLER. Vol. I. *(Philadelphia: W. B. Saunders & Co., 1906.)*

The book, including the index, comprises 722 pages, with 398 text illustrations and four colored plates. The paper is good, the type large and clear, the illustrations well executed, and altogether the mechanical construction of the book is very creditable.

The author states in his preface that he will treat the subject of surgery under what he designates as the Anatomic Method, that is, the consideration of injuries and diseases as related to each particular region. This is the same method which was followed by Koenig.

The first chapter, on Inflammation, includes Surgical Bacteriology and a short discussion of Sterilization and Aseptic Technique. This chapter in many parts is incomplete and the illustrations comprise those of ordinary sterilizers, incubators, etc., which are well known to every second-year student.

The section on "Laboratory Aids" includes a synopsis of the examination of the blood, urine, feces, gastric contents, etc. Illustrating this chapter one finds the ordinary blood-estimating apparatus, the freezing microtome, and other things equally elementary. To any one who is familiar with clinical microscopy such a short consideration will be of no value, and to others who are not so well grounded his descriptions are too cursory to be of any material aid. In a discussion on leucocytosis it is his opinion that the increase of leucocytes in general indicates a resistance on the part of the patient rather than any special local condition. In order to arrive at an idea of what has taken place at the point of infection an estimation of the polynuclear neutrophiles must be made. From an examination of over 1400 blood counts he has found the normal to be 70 per cent. Above this number he interprets as indicating the presence of pus; below this number pus or gangrene are excluded. An increase of the polynuclear neutrophiles with little or no inflammatory leucocytosis indicates an inflammatory process, together with little resistance on the part of the patient. The same increase with a high inflammatory leucocytosis means good resistance. In this chapter he has given two cuts; one of tubercle bacilli and another of smegma bacilli. The tubercle bacilli are beautifully arranged in regular lines and curves; the smegma bacilli irregularly scattered in patches. Such a distinction, no doubt often occurs, but not sufficiently so to make this any special point in differentiating them.

Anæsthesia is well treated, but too little is said about Nitrous Oxide Gas and Ethyl Chloride.

In the section on General Principals of Operative Technique he has followed the same course of illustrating the simplest surgical instruments; knives, dissecting forceps, saws, curettes, etc. In modern surgical education a student becomes familiar with these instruments by seeing them and not by their illustrations in a book.

The discussion of Tumors is done in a very general manner and so extremely cursory that it has not much value.

The general consideration of Bone Diseases is incomplete.

Syphilis and Tuberculosis are treated in a short and elementary manner, for such important subjects.

The book presents very little that is new and is cumbered by so many unnecessary illustrations, incomplete chapters and descriptions of unnecessary detail that it is questionable if it is any addition to surgical literature.

Prevalent Diseases of the Eye. By SAMUEL THEOBALD, M. D. *(Philadelphia: W. B. Saunders & Co., 1906.)*

The teaching of the special branches of medicine has assumed a rank of growing importance at our medical schools. There are those still in practice who in their student days had the entire scope of theory and practice covered by the "five chairs." Later on the many "ologies" claimed recognition and so during the past half-century, the length of the course of study was doubled, but the separate branches taught increased fivefold. With this growth in the number of separate studies, there has been little effort at coordinating them. The teaching of the different branches, as reflected in the numberless text-books, has been apparently guided by the purpose of furnishing the student with a more or less condensed supply of the entire subject, varying between the limits of the inadequate compends and the ponderous hand-book. And yet it has been the object of the medical school to prepare the vast majority of its graduates for general medical practice. Considering the vastness of the field, it would appear quite as important that the teachers of the specialties should study carefully to exclude that which is unimportant, not in itself, but from the point of view of the needs of the general practitioner, as to teach that which is important. For it need scarcely be added, that while much of the knowledge of a specialist would be ornamental only to the general practitioner, there is that which is not only useful but essential. And just as the teacher must use the art of selection, so the text-books, which are designed for the student and the medical practitioner, should be adapted to their needs. Of no specialty can it be said more truly than of ophthalmology that "of making many books there is no end," and yet few measure up, even partially, to the requirements as just outlined.

In the recent book of Dr. Theobald, "Prevalent Diseases of the Eye, a reference hand-book, especially adapted to the needs of the general practitioner and the medical student," the attempt has been made to meet this demand of the general practitioner "by taking into account the fact that the great majority of physicians are not skilled in the use of the ophthalmoscope, and are not likely ever to be; that they possess neither the experience nor the necessary paraphernalia to make trustworthy tests of refractive errors, of muscular anomalies, or of the visual fields; and that they are not qualified to perform, and have no desire to undertake, the more delicate eye operations . . . . but, on the other hand, that there are other important affections of the eye which he is competent, or should be competent, to diagnosticate correctly, and to treat successfully."

The book is admirably written, with great clearness, reads smoothly, and is specially interesting because it records the wide experience of a careful and observant practitioner. It is refreshing to read a new text-book which is evidently not a simple compilation of those that have gone before. The illustrations are numerous and clear, the colored ones, mostly original, are especially vivid.

The chapters on general observations upon the diagnosis of diseases of the eye; description of the methods of examining the eye available to the general practitioner; general observations upon the treatment of diseases of the eye; and those devoted to the external diseases including diseases of the iris, are admirable. The chapter on anomalies of refraction and accommodation gives good advice concerning the prescribing of glasses, advice it would be well for many physicians to read.

In some matters the work does not follow the accepted views, the differences being based upon the experience of the author. He has succeeded in laying stress upon the subjects which are of importance and eliminates that which is unimportant. The book

is filled with helpful hints, for the author does not despise minutiæ, and it will certainly prove useful and become a popular work of reference to the physician in general practice.

H. F.

International Clinics. Vol. I. Series 17. 1907. (*Philadelphia and London: J. B. Lippincott Company, 1907.*)

In addition to a number of interesting papers on treatment, medicine, surgery, gynæcology, ophthalmology, and laryngology, more than a hundred pages of this volume are devoted to the progress of medicine during 1906. As a historical review of the advances made, and the constant change of opinion and practice in various branches of medicine, this final chapter is perhaps the most important in the book. The first article "On the Psychic Treatment of Some of the Functional Neuroses" by Dr. Lewellys F. Barker is, however, one of equal value from another point of view. These troubles are to-day being studied with more care than ever before, and are securing the proper attention which, through ignorance and misunderstanding of their importance, they long failed to obtain. To save a neurasthenic or hypochondriacal patient from becoming insane, or to rescue the so-called "border line" sufferers, and restore them to a normal frame of mind is of more value to the community than to cure a case of pneumonia or typhoid fever. It is, therefore, necessary that as much study be paid to the "functional neuroses" as is now spent on other more acute diseases. Every authoritative article, therefore, is to be welcomed, and it is satisfactory to note that the "International Clinics" begin their new series with a contribution to this subject.

R. N.

The Diseases of the Nose, Throat, and Ear. By Charles Prevost Grayson, A. M., M. D., Clinical Professor of Laryngology in the Medical Department of the University of Pennsylvania, etc. Second edition, revised and enlarged. (*Philadelphia and New York: Lea Bros. & Co., 1906.*)

We take pleasure in recommending the second edition of this well-known work to students and practitioners of medicine. It is hardly comprehensive enough to be classed with the larger works devoted to special practice, but is most useful as a reference book for those who have not the time to consult the more exhaustive works. The sections devoted to local treatment are of especial value.

We cannot agree with the author in some of his statements. He decries the use of cocaine solutions of greater strength than 8 per cent. We have found that one cannot get nearly as satisfactory anæsthesia with such solutions as with the powdered cocaine, especially in the case of operation on the sinuses.

We would like to call the author's attention to the incorrect use of the term myxoma in the chapter on growths in the nose. He uses this expression in describing the common mucous polyp found in the nose. Myxomata are the rarest of all tumors found in the nose, mucous polypi the most frequent. The fluid content of the mucous polyp is not mucin but a serous exudate and the technical name of the mucous polyp is edematous fibroma.

The chapters on ear diseases are fairly satisfactory. We regret that the author has not seen fit to describe in a separate chapter the fairly common disease known as otosclerosis. This differs in several important ways from the frequently seen chronic aural catarrh. The middle ear is not affected with the exception of the stapes, which is united by spongy bone to the oval window. This disease usually starts between the twentieth and thirtieth years of life with gradual loss of hearing and tinnitus. It should be sharply differentiated from the catarrhal condition as the prognosis in the latter is so much more favorable.

Sylvan Rosenheim

Department of Neurology: Harvard Medical School. Vol. II. Boston, Mass., U. S. A., 1907.

From this department there has just appeared a second series of contributions by such well-known neurologists as Putnam, Knapp, Walton, Taylor, and others, dealing with hysteria, cerebral and cerebellar tumors, injuries to the skull and cord, multiple sclerosis, exophthalmic goitre, tabes, and psychotherapeutics. The collection of papers published in various journals which all deal with one branch of medicine is to be commended, and these volumes from the Harvard Medical School, with a similar volume lately published on "Tumors of the Cerebrum," by Dr. Mills and others in Philadelphia make most interesting additions to American neurology.

R. N.

Epitome of Pathology. By John Stenhouse, M. D., and John Ferguson, M. D. (*Philadelphia and New York: Lea Bros. & Co., 1906.*)

This little book of 265 pages is intended to be an epitome of general and special pathology. The section on general pathology has a few fairly good illustrations. The subject matter is chiefly clinical chemistry and microscopy, and for the most part is little more than a dictionary. The second part on special pathology states briefly the etiological factors of and the anatomical findings in the various diseases. If the authors had been more careful with their English, the book would be more valuable, since a person knowing little of the subject would certainly be considerably misled in many instances. The authors have also made bad mistakes in stating the size of the various intestinal parasites (see page 92).

Talks to First-Year Nurses. By Alfred T. Hawes, M. D. (*Boston: Whitcomb & Barrows, 1907.*)

As the author says in his introduction "the following talks are elementary in character, and are not to be considered as thorough discussions of the subjects of which they treat. The details are to be filled in by subsequent studies and courses of lectures. The design of these talks is to give nurses enough information to enable them to understand the general condition of their patients and to carry out intelligently the details of their work."

Although many primers or hand-books for nurses have been published, yet there are but one or two really first-class ones, and this small book cannot be considered to rank with the best. It is too "elementary" and does not give "enough information." Too many subjects are cursorily handled and it is not altogether well arranged. In one respect it resembles too closely a dictionary in simply defining names and terms. Its few illustrations are poor. The author's style is clear and simple, but in attempting to be simple and brief he has cut his work too fine, and so failed to produce a really serviceable guide.

R. N.

The Prophylaxis and Treatment of Internal Diseases. By F. Forchheimer, M. D., Professor of Theory and Practice of Medicine and Clinical Medicine, Medical College of Ohio. (*New York and London: D. Appleton & Co., 1906.*)

There is undoubtedly a demand for a good work on the prophylaxis and treatment of internal diseases. Many students and practitioners, particularly recent graduates, feel the need of more detailed information than that which can be given in the usual text-books of medicine.

In the present volume the subject-matter is treated in the usual sequence and the individual topics are, as a rule, discussed at length. As in most first editions, all is not as the author may have intended. The treatment of "typical" lobar pneumonia is well given. Separate consideration is given to "atypical" pneu-

monia; the author says: "All forms of lobar pneumonia belong to this type when their course varies from that of the normal as to the duration, intensity, complications, and the individual attacked"—clearly a too elastic definition, one which, we should judge, might be made to include the majority of all cases of lobar pneumonia. In the atypical pneumonia "quinine, given by the mouth or subcutaneously, is of decided value"—a statement to which many would take exception. Though the author has not used the drug himself, it is disappointing to find reference made to creosote carbonate which has been of no value in the hands of most careful observers. That "adults need never be immunized" against diphtheria is doubtless an erroneous view and one which, if followed, would lead to serious consequences. In the prophylaxis of rheumatic fever the value of removal of the tonsils has been overlooked, though this may have been purposely omitted because of the lack of satisfactory statistics upon which to base judgment. The classification of diseases of the stomach is confused, particularly that relating to the gastric neuroses. Under motor neuroses the only condition treated of is cardiospasm, while peristaltic unrest, nervous vomiting, regurgitation, etc., are placed under the secretory disturbances. The nervous form of achylia gastrica is generally recognized, but "cancer, tabes, and sclerosis of the stomach" are not so generally accepted as causes of it. The chapter on chronic myocardial insufficiency is one of the most illuminating in the book. Here the author is seen at his best. The subject is handled excellently, the various methods of physical therapy are splendidly discussed, and the advice given seems thoroughly sound in all respects. Criticism might be made of the use of the word "decompensation" for the usual "incompetency"—a minor point—but, aside from this, it is difficult to see how the text could be improved. Certainly great good would result if all practitioners could read and profit by what the author has to say on chronic myocardial insufficiency. Treatment of tetany with thyroid extract is irrational therapeutics, and from the excellent results reported in the few cases where parathyroid glands have been tried, they should be administered in this symptom-complex. Neurasthenia, one of the commonest—perhaps the commonest—of diseases, is unintelligently or unsympathetically treated by the majority of physicians, it is safe to say. While it must necessarily be considered within the limits of a few pages in a work of this size, the space has been very advantageously used and the teaching is, we believe, helpful.

As in all of Appleton's works, a good quality of paper is used, the type is easily legible and clear, and the book is attractively put together.

A Text-book on the Practice of Gynecology. By WILLIAM EASTERLY ASHTON, M. D., LL.D. Third edition, revised and enlarged. (*Philadelphia and London: W. B. Saunders & Co.*)

The third edition of this work on the practice of gynecology has been demanded inside of a year. This tribute to its worth speaks for itself. The present third edition has received a thorough revision by the author, and many beneficial changes have been made. The general plan of the book for teaching purposes is excellent. Dr. Ashton has followed a definite routine in his consideration of each subject, taking up the different phases of each disease in a definite order. Such an arrangement is always helpful to the student.

In a practice of gynecology such as this book is, one could hardly expect to find long chapters on the fundamentals, such as embryology and pathology. However, as both of these subjects, especially the latter, are at present so intimately connected with the actual practice and operative procedures in gynecology, it seems as though some mention should be made of the pathological changes. One might almost say that instead of the minute descriptions of operating rooms and operative technique, which can never be learned from a book but only by actual practice in the operating room, possibly that space might have been used in brief descriptions of the pathology of gynecological affections.

The chapter on cancer is very full, and strongly emphasizes the important points in the diagnosis of this disease. The early symptoms are plainly stated and their importance is insisted upon. Clear statements such as Dr. Ashton makes in this chapter on the recognition of cancer are the very words needed to train the general practitioner and the student to bring cases of cancer of the uterus early to operation.

Each disease of the pelvic structures has been treated separately and distinctly, and there has been no lumping of subjects with many subdivisions. This feature of the book is especially satisfactory and prevents confusion in looking up any one subject.

The chapter on cystitis is excellent, especially the differentiation of the various kinds of cystitis, separating them one from the other clearly.

In the chapter on tuberculosis of the pelvis, perhaps more stress might be laid on the radical operations for tuberculosis. Pathology shows us that tuberculosis of the tubes and ovaries rarely occurs without the involvement of the uterus, especially the endometrium. Dr. Ashton advises complete removal of the pelvic structures when there is present macroscopic evidence of involvement of the uterus. However, as the tubes and ovaries are so seldom, if ever, involved by tuberculosis with uterus remaining free, it seems that the greatest chance for a cure would be by the complete removal of the entire pelvic structures in *every* case of pelvic tuberculosis.

The chapter on the anatomy of the pelvic floor is especially important, and the illustrations, while somewhat diagrammatic, are clear and helpful.

The book is a satisfactory one from the standpoint of the student and the general practitioner, for whom it is written, and forms a good every-day reference book for workers in the gynecological field. H. T. H.

Anatomical Terminology with Special Reference to the BNA. By LEWELLYS F. BARKER, M. D. (*Philadelphia: P. Blakiston's Son & Co., 1907.*)

The need for a consistent, methodic, and exact system of terms used in designating anatomic parts and their position has been felt by many teachers and investigators. Recent advances in anatomy have been attended by many changes in nomenclature and anatomic names have accumulated in such large numbers that our lexicology has become tremendously overburdened. It is a strange trick of the vicissitude of things terminologic[1] that the reform movement initiated as it was on this side of the Atlantic in the early '80's under the leadership of Wilder, Leidy, and others should result in the production of a list of terms adopted by the "Anatomische Gesellschaft" of Germany in 1895 under the title of "BNA" and in this year of 1907 to be brought, more effectually, we trust, to the attention of American students under the editorship and with the stamp of approval of Professor Barker. In the preface of this book we find the history of the work done by the German Commission up to the time of the adoption of its list at the Bâsle meeting. Rather scant reference is made to the prior revisions undertaken by committees of the American Association for the Advancement of Science, the Association of American Anatomists, and the American Neurological Association. In this connection Professor Barker expresses the hope that "at another revision, the terms in Professor Wilder's lists which differ from those of the 'BNA' may be carefully considered, and that his terms, where they are better than those of

[1] *Terminology* is a hybrid Latin-Greek word (as are many of the "BNA" terms) and should be replaced by *nomenclature*. For other philologic reasons, *anatomic* is preferable to *anatomical*.

the present 'BNA,' may be adopted." While we disclaim all desire to revive the animadversions of a past controversy, it must be pointed out that this is written more than a decade after the American pioneers in the reformation of anatomic nomenclature met with rebuff, even discourtesy, at the hands of certain members of the very commission which formulated the "BNA."

In the pursuit of its work the Commission adopted certain general rules of simplification which are in the main excellent ones. Thus "(1) each part shall have only one name; (2) each term shall be in Latin and be philologically correct; (3) each term shall be as short and simple as possible; (4) the terms shall be mere memory signs and need lay no claim to description or speculative interpretation; (5) related terms shall, as far as possible, be similar—e. g., *Femur*, *Arteria femoralis*, *Vena femoralis*, *Nervus femoralis;* (6) adjectives, in general, shall be arranged as opposites—e. g., *dexter* and *sinister*, *major* and *minor*, etc." .

A divergence of opinion among the members of the Commission with regard to the use of personal names was compromised by putting the widely used ones in brackets after the objective name—e. g., *Lig. inguinale* [*Pouparti*]. The Commission did not adhere strictly to this rule as shown by the terms *Corpus Wolffi*, *Ductus Wolffi*, and *Ductus Muëlleri;* unwarranted terms we think, in the case of the first two at least, since morphologists have long employed *Mesonephros* and *Mesonephric duct*. While in the "BNA" the older *Foramen of Winslow* is correctly replaced by *Foramen epiploicum* (ἐπίπλοον = omentum) we question the correctness of the term *Appendices epiploicæ* (p. 48), structures which have nothing to do with any omentum.

Although the Commission adopted the general rule that "each term shall be as short and simple as possible" we do not find this resolve carried out to the most desirable extent in many instances. The attending difficulties may be of natural origin since the German-speaking anatomist enjoys the facile enunciation of such terms as "Atrioventrikularverbindungssystem," "Brustschlüsselzitzenfortsatzmuskel," and "Zwischenkiemendeckelstück." That the "BNA" terms chiefly lack the attribute of brevity may be seen in their comparison with certain terms in Wilder's lists, tabulated here below, and more or less extensively used by leading American teachers and investigators:

"*BNA*."	*Wilder*.
Calvaria	Calva.
Chiasma opticum	Chiasma.
Nucleus dentatum	Dentatum.
Corpus pineale	Epiphysis.
Medulla spinalis	Myelon.
Medulla oblongata	Oblongata.
Corpus striatum	Striatum.
Corpus callosum	Callosum.
Calcar avis	Calcar.
Falx cerebri	Falx.
Falx cerebelli	Falcula.
Tentorium cerebelli	Tentorium.
Dura mater	Dura.
Pia mater	Pia.
Splenium corporis callosi	Splenium.
Vena cava superior	Præcava.
Vena cava inferior	Postcava.
Substantia corticalis	Cortex.
A. cerebri anterior	A. præcerebralis.
Nucleus amygdalæ	Amygdala.
M. latissimus dorsi	M. latissimus.
Foramen interventriculare (Monroi)	Porta.

With Wilder we prefer to drop the substantive *corpus* used in combination with *callosum*, *striatum*, *albicans*, etc., retaining it only when it plays the part of a useful adjective as in *corpus fornicis*, *corpus epididymidis*. To drop the noun and employ the adjective substantively, as in *pia* mater, membrana *mucosa*, tunica *serosa*, substantia *cinerea*, is no innovation, for in the article "Cerebrum" in James' Dictionary, published in 1743, we find *pia* used alone. If we are to employ the dionym *dura mater* we cannot consistently use the term *cavum subdurale* recommended by the "BNA."

How burdensome the use of polyonyms has become to medical men and others engaged in anatomic study is shown by the general use of *Cecum* (*cæcum* = "closed") in place of *Caput cæcum coli;* of *Tentorium* without the needless *cerebelli*, and of *Cortex* instead of *substantia corticalis* in several organs. A further potent argument in favor of mononyms, whenever these can be adopted, is suggested by the abbreviations to which they so readily lend themselves in articles and figure-legends written in different languages. Thus, as Wilder has pointed out, the dionym *commissura anterior* would be *c. a.* in the Latin and French, *a. c.* in the English, and *V. C.* in the German; but of the mononym *præcommissura* the abbreviation *prc.* would probably serve in either case and render its recognition by foreign readers easy. Not only do such mononyms lend themselves to more uniform abbreviation, but adjectives may be more readily derived, the names are more readily compounded, and by paronymy more easily adopted into other languages.

The two terms *crus* and *pedunculus* are used convertibly, without consistency, in many modern text-books. Thus, it is common to read that the *crura cerebri* enclose the *interpeduncular space*. As has already been said [2] it would have been better if anatomists had agreed to use *crus* only for the cerebral tract and *pedunculus* for the cerebellar, with, of course, the modifications made appropriate by the terms *præpedunculus*, *medipedunculus*, and *postpedunculus*. The word *pedunculus*, by the way, is not included in the list of general anatomic terms on p. 16.

While mononyms are to be preferred, no sensible anatomist would insist upon their adoption at the risk of ambiguity, and why *utriculus* should stand alone in the "BNA" list of structures of the internal ear, and be compounded with *prostaticus* in the list of structures in the male urethra is not explained. By the context we may understand which *vestibulum* (unaccompanied by any adjective) is meant under *Labyrinthus osseus* on p. 92, but on pp. 45, 50, 52, 57, and 59 we see the compounds *vestibulum oris*, *v. nasi*, *v. laryngis*, *v. vaginæ*, and *v. bursæ omentalis*.

Although it is claimed that the "BNA" list "consists chiefly of carefully selected old names" we find new, or at least comparatively unfamiliar names given to several carpal bones and the *torcular* is called *confluens sinuum*. The old *M. zygomaticus minor*, *M. levator labii superioris*, and the *M. levator labii superioris alæque nasi*, formidable enough as they were, are grouped under the general term *M. quadratus labii superioris*, with a *caput zygomaticum*, *c. infraorbitale*, and *c. angulare*, corresponding to each of the above-mentioned facial muscles. McMurrich has shown the incorrectness of this classification from the morphologic standpoint.[3] Inasmuch as our anatomic vocabulary should be applicable to all vertebrates it were better, as Wilder has suggested, to employ *M. ectopectoralis* and *M. entopectoralis* for the two frequently named muscles whose relative proportions in most mammals are so misrepresented by the adjectives *major* and *minor*. On similar morphologic grounds the terms *Præcava* and *Postcava* are preferable to *Vena cava superior* and *Vena cava inferior*, and *Præsternum*, *Mesosternum*, and *Xiphisternum* are better and more generally applicable than the *Manubrium sterni*, *Corpus sterni*, and *Processus xiphoideus* of the "BNA." In speaking of the *cinerea* (*grisea* or gray matter) of the myelon the terms *Cornu dorsale* and *Cornu ventrale*, adopted by the various American associations mentioned above, are preferable to the "BNA"

[2] E. C. Spitzka, Science, April 9, 1881.

[3] Amer. Jour. Anat., III, 1, Proceedings, p. iii.

terms of *Columna posterior* and *Columna anterior* on account of their different relations in prone and erect animals. The same objection is to be offered against *posterior* and *anterior nerve-roots*, instead of the more exact *dorsal* and *ventral*. This disregard for the needs of comparative anatomy constitutes a serious imperfection in the work done by the German Commission.

The second rule adopted by the Commission reads that "each term shall be in Latin and be philologically correct." In referring to certain adjectives employed in the "BNA" which end in *-icalis*, a diligent search through Freund's Latin-German Lexikon, edited by Charlton T. Lewis and Charles Short (Harper's Latin Dictionary) fails to reveal any such termination and with regard to specific instances we find each such "BNA" term to be incorrectly constructed:

"*BNA.*"	*Classic Latin.*
Annulus umbil*icalis*	A. umbil*icaris*.
Fovea supravesi*calis*	F. supravesi*caria* (*-ius*).
M. lumbri*calis*	M. lumbri*cosus*.
Substantia cort*icalis*	S. cort*icatus*.
Plexus cervi*calis*	Pl. cervi*catus*.

The word *cervical* (also *cervicale*) is a noun which is defined as a pillow or bolster, but there is no adjective so spelt.

There are few errors of omission. Among these we may suggest the bundle of "Purkinjé fibers" in the heart which received the attention of Purkinje and the younger His before the "BNA" was adopted, and which has since been more exhaustively investigated by Tawara, Retzer, and others under the name of *Atrioventricular bundle*. The insertion of *Foramina venarum minimarum* (*Thebesii*) under the list of structures in the right atrium of the heart only, seems to imply that these foramina are present in this chamber of the heart alone, whereas Thebesius, himself, mentions their existence in all of the heart chambers (1708). The ontogenetic term *Foramen ovale* should be included on p. 60, and, *Pronephros*, *Mesonephros*, and *Metanephros* on p. 58. Only one *Duodenal papilla* is mentioned. On p. 74, under "Sectiones Medullæ spinalis" we find no mention of the *Fasciculus marginalis*, or *Fasciculus dorso-lateralis*, discovered simultaneously by Lissauer and E. C. Spitzka (1886) and usually bearing the name of the former.

The Latin terms, "the only authorized ones," are accompanied by an English vocabulary which Professor Barker offers tentatively and as "simply explanatory." This caution is wisely proffered and is always to be borne in mind; for we read that *Uvula* is a *little cluster or bunch* (p. 16), *Axilla* is the *prominence of the shoulder* (p. 18), *Alveoli dentales* are defined as *tooth cavities* (instead of tooth sockets) (p. 25), while the term *tooth-cavity* is correctly given for *Cavum dentis* on p. 46. Professor Barker prefers *Carotid skein* as the English equivalent for *Glomus caroticum* (p. 53.) The literalness of the translation is at times carried too far, as, for example, in *Deep artery of the thigh* for the *A. profunda femoris* (p. 67), *Lozenge-shaped brain* for *Rhombencephalon* (p. 74), and *Writing pen* for the *Calamus scriptorius* (p. 75). It would have been better to repeat the terms *Clava* and *Obex* in the English column and put the definitions *Club* and *Bar* in parenthesis. The same with *Blue place* and *Black substance* as the equivalents of *Locus cæruleus* and *Substantia nigra*, the last-mentioned term being, in our opinion, not quite so good as *Intercalatum*.

We regret to see *Ammon's Horn* perpetuated (p. 80) even though it be only in the category of old terms; for the *Cornu Ammonis* (now designated by the better term *Hippocampus*) was not named after a man named Ammon. The erroneous form probably arose from a thoughtless translation through many past decades, of the vernacular *Corne d'Ammon* in the French, *Corno d'Ammone* in the Italian, and *Ammonshorn* in the German. We also notice the repetition of the old term *Steno's duct* (p. 46). If the term *Parotid duct* is to be at all accompanied by the name of its discoverer it should be correctly given, for it was Nickolas Stensen whose name is associated with this structure in the latinized genitive *Stenosis*.

Professor Barker shares the feeling of the members of the "Anatomische Gesellschaft" that the "BNA" is after all a provisional list and one which in that capacity has accomplished much in "clearing the decks for action." The list as it is now constituted offers much for reflection, debate, and renewed revision. It still contains stumbling-blocks for students of Anatomy and it stands in need of considerable simplification and application to comparative anatomic considerations. In the list of forty terms adopted by the American associations, twenty-five are identical with those of the "BNA" while the remaining fifteen are each and all shorter and more appropriate. With so much as a nucleus, and with the spirit of word-simplification animating the present generation, we may hope to see anatomic terminology formulated upon more logical and satisfactory lines of word construction and endowed with more lasting qualities.

EDW. ANTHONY SPITZKA.

Organic and Functional Nervous Diseases. By M. ALLEN STARR, M. D. Second edition. (*New York and Philadelphia: Lea Brothers & Company, 1907.*)

The first edition of Dr. Starr's valuable text-book appeared in 1903. The present edition offers in addition to a revision of the original text, a section of seven chapters on functional diseases of the nervous system, thus making the volume larger by sixty-five pages than the preceding one.

In the first part, on organic diseases, there are but few alterations. These consist for the most part of brief additions here and there of later observations by the author or others in symptomatology and treatment. In the histologic section two new cuts appear illustrating the disposition of the neurofibrils in the ganglion cells, and the epicellular end-structures. Two plates, originally in black, showing various normal and pathologic conditions of the nerve-cell, are attractively printed in blue monochrome. In the chapter on motor localization two new brain maps have been substituted for the old ones and the common error of locating the motor centers on both sides of the fissure of Rolando has been corrected. The treatment of the pathologic histology of paresis is hardly up to date, and cytodiagnosis as a differential diagnostic procedure receives scant notice.

The supplementary section on functional diseases treats in order the spasmodic neuroses, epilepsy, paralysis agitans, tetany, neurasthenia and occupation neuroses, hysteria and migraine, and presents six new illustrations.

The book is doubtless the best of its kind which has appeared in this country.

Saint Bartholomew's Hospital Reports. Vol. XLII, 1906. (*London: Smith, Elder & Co., 1907.*)

The value of these reports has long since been well established, and it remains but to welcome each new volume. This one contains several papers of importance, a thesis on hypertrophic pulmonary osteo-arthropathy, with a complete bibliography of this rare disease, and an article on "some diseases of the blood in children associated with enlargement of the spleen," to mention but two in the desire of attracting students to search the volume for themselves, and discover other equally noteworthy articles.

R. N.

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A BRIEF REPORT OF THE FIRST TWO YEARS' WORK IN THE PHIPPS DISPENSARY FOR TUBERCULOSIS OF THE JOHNS HOPKINS HOSPITAL.

By Louis Hamman, M. D.

The Phipps Dispensary of the Johns Hopkins Hospital, established through the generosity of Mr. Henry Phipps, was formally opened on February 21, 1905, and the first patients received on March 1 of the same year. The work has gradually increased in extent and grown in usefulness. During the first year 639 patients were registered; during the second 835, and from two physicians and a nurse, the staff has grown to ten physicians and still only one nurse, but by joining forces with the two other tuberculosis nurses in the city, the work of the nurse has developed in a most satisfactory and valuable manner.[1] With the gradual increase in assistance, it has at last become possible to begin in an humble way plans which were from the beginning hopefully formed, but which could not be carried out on account of the great amount of routine work. Much, however, remains to be done, and this report is but an indication of a tendency which it is hoped will gradually branch into a much wider field of usefulness. There are several aspects of the work, which it is best to consider separately.

The main function of a tuberculosis dispensary is the prevention of the spread of the disease, a campaign of prevention by education, by education taken in its broadest sense. We are more and more impressed with the importance of the home as a center of infection and the figures so carefully gathered, which Dr. Hazen will report, are astonishingly corroborative of this fact. It is impossible to follow Koch's suggestion to remove these cases, as the most efficient means at our command to check the spread of the disease, but something at least, can be accomplished by rendering them relatively harmless. It is as useless simply to tell a patient, and particularly an ignorant patient without means, to burn his sputum and use paper napkins, as it is to tell him to go to the country and eat plenty of eggs and drink plenty of milk. In both instances the principles are sound, but to attain results demands an endless and untiring application in detail of the principles. This is the work of the nurses, to follow the patients to their homes, not alone to tell them what to do, but to show them how to do it; to return week after week to see that their instructions are being carried out, and to demon-

[1] There are at present three nurses engaged in the work in the city. Miss Spicer, who is directly connected with the Phipp's Dispensary and is supported through the generosity of Mr. Bloede, Miss La Motte, supported by private contributions secured by Mrs. William Osler, and Miss Bond, supported by the Graduate Nurses' Fund. Their heavy task is best measured by the statement that they have a permanent visiting list of about 700 patients.

strate to them, if necessary again and again, what to do. This is the most important service of a dispensary and its value is so well recognized in Germany that at the tuberculosis relief stations the physicians do little but diagnose the cases, and give general directions for treatment. The painstaking and often discouraging labors of the nurses are performed in such a quiet, unobtrusive way that they frequently do not obtain from the public their due recognition. This is the work that tells, however. Dr. Forster can show that many cases have been cured at Eudowood and that in many patients the disease has been arrested, but it is impossible to show that Miss Spicer's results are still better, for although she has saved many persons from contracting the disease, this cannot be statistically demonstrated. We know, however, that this is a fact. The nurses have been of the greatest assistance in other ways. They have followed the doubtful cases and have insisted upon their return to the dispensary from time to time for further observation, and they have encouraged a large number of patients to come to us for examination who have been or are being continuously exposed to the disease. It is to their zeal in this direction that we owe the discovery of some of our earliest cases.

Education is further disseminated by the patients themselves among their friends, and indeed in their whole neighborhood. One of our patients in particular has carried on an active personal propaganda and has herself brought in 12 others for examination, and among these there have been two early cases. A number of patients who are sleeping out of doors have aroused the curiosity and interest of their neighbors, and it is to be hoped their confidence also in the treatment. The staff of physicians have also assisted in a modest way in the work of education, with encouragement and advice. Many have responded to invitations from the Society for the Prevention of Tuberculosis to speak before various clubs and societies. Certainly a great deal more could be done in the instruction of every medical student here and elsewhere, but the facilities for this are inadequate. Each student should at least be able to make a careful physical examination and to give tuberculin with safety. At present the Phipps Dispensary here furnishes a large portion of the teaching material for the third year students of the Johns Hopkins Medical School. In a small way the work of this Dispensary is being recognized outside of its immediate sphere of activity. The Charity Organization Society frequently seeks its aid and a few physicians send to it their patients for examination and advice. The second important aim of the dispensary is to consider the individual and try to do something for him. During the first year this was necessarily almost entirely disregarded, but during the past twelve months, and particularly during the past six, more and more has been attempted. The first duty in this direction is careful and efficient diagnosis, so that the cases that come to us may be recognized in the very earliest stages and placed at once under proper control. It is remarkable how even advanced cases will improve under proper conditions, but in the dispensary class of patients a return to the surroundings under which the disease was contracted inevitably means relapse. The results are really satisfactory only when the disease is diagnosed early, and as far as our short experience goes, in such cases the outcome promises to be very encouraging. The proper disposition of these early cases has become possible in the past year through the close affiliation of the dispensary and Eudowood Sanatorium. This close association of the two institutions is very gratifying to us, as by its means our sense of responsibility towards these patients is greatly aided. We are seeing more and more early cases, and we feel that we are becoming more and more proficient in diagnosis, especially since we have been able to use tuberculin more extensively.

We are able to do very little for our advanced cases. The only provision made for their care is the City Hospital at Bay View, and many of them refuse to go there. We feel constantly and urgently the need of accommodations for dying patients, not alone as a charity to the individuals themselves, but as the most efficient barrier we have to the further spread of the disease.

We have at last been able, with the aid of more assistants to satisfy a long-felt desire to do something more definite for the ambulant moderately advanced cases and for the early cases unable to find accommodation at Eudowood. In December, 1906, a small class of five or six patients was formed, whose home conditions were to be more vigorously controlled and their whole mode of life more carefully regulated. At the same time, stimulated by the enthusiastic reports of the use of the specific products of the tubercle bacilli, we instructed the patients how to keep careful records of their temperature, pulse, and symptoms preparatory to giving tuberculin injections. In January, 1907, such injections were begun and have been continuously employed since then, only the old tuberculin being used. The class has gradually grown to over 20 members. In this work Dr. Denker has rendered invaluable assistance, giving largely of his time and means in improving the home conditions of the patients. At first the patients records were kept in simple notebooks, more recently copies of the books used by Dr. Pratt in Boston have been furnished the class by Dr. Denker. It is too early to say anything about results, other than to state that a majority of the patients have improved in a most satisfactory manner. Of course there are a good many difficulties in the way. The patients must be selected not only with a view to their personal fitness, but with regard to their home conditions. There must be some foundation to build upon. Many of the patients too do not respond as whole-heartedly to our advice as we wish. It requires much persuasion and encouragement to induce them to accept the necessary routine. Many are still unwilling to do all we ask of them, but we are gradually controlling them better. The influence of one patient upon another is often far more effective than anything we can say or do, and we frequently turn a new member over to the guidance of an old, intelligent pupil with gratifying results. It is too soon to exact that all the details we suggest be strictly fulfilled, but as the work enlarges, we shall be able to demand a rigid adherence as the price of enjoying the privileges membership in

the class confers. We must first of all make such privileges apparent. What do we propose to accomplish by such a plan as I have suggested? It is our intention to treat those patients who cannot find accommodation in sanatoria where advanced cases are usually rejected. Here is a feature in which the home treatment has an advantage over institutional, for the home becomes the sanatorium and the patient, if he recovers, is prepared to live for the rest of his life in a great measure under the same surroundings to which he has long been accustomed. This is a more important matter than it would seem at first glance. The results which have been obtained in the advanced cases at Towson, where they live practically out-of-doors, have been temporarily splendid, but we have seen regretfully relapse after relapse quickly follow the return of these patients to their homes in the city. They have not appreciated that they might follow at home the same life they have led at the sanatorium. We mean to teach these home-returning patients how to practice the same principles they have followed in the sanatorium. We have in our class at present four former Eudowood patients who have had a return of symptoms. Another important object of the class is to spread our teaching through the patients themselves, and thus educate the public still further.

Statistics.

During the first year 639 patients were admitted; during the second year 835, giving a total of 1474 patients. Of this number:

956, or 65%, were cases of definite pulmonary tuberculosis;
204, " 13%, were doubtful cases of pulmonary tuberculosis;
245, " 17%, were cases other than tuberculosis;
28, " 2%, were tuberculous cases other than pulmonary;
41, " 3%, of the histories are too incomplete to be considered.

Of the 28 cases of tuberculosis other than pulmonary:

7 are glandular tuberculosis,
7 " pleurisy with effusion,
7 " fibroid pleurisy,
3 " tuberculous peritonitis,
1 is tuberculous pericarditis,
1 " bone tuberculosis,
1 " tuberculous cystitis,
1 " tuberculous adenitis and arthritis.

Of the 245 non-tuberculous cases:

14 had bronchitis and emphysema,
12 " adenoids,
14 " valvular disease of the heart,
3 " lobar pneumonia,
6 " bronchiectasis,
3 " bronchial asthma,
3 " typhoid fever,
2 " Basedow's disease,
2 " empyema,
2 " syphilis,
2 " arteriosclerosis,
1 " pharyngeal catarrh,
1 " nasal obstruction,
1 " carcinoma of the stomach,
1 " chronic interstitial nephritis,
1 had hysteria,
1 " purpura rheumatica,
1 " alcoholic gastritis,
1 " muscular dystrophy,
1 " arthritis deformans,
1 " laryngitis.

In the other cases the examination was negative and no definite diagnosis was made. The large number of doubtful cases is principally due to the frequency with which patients make only one or two visits to the dispensary. Many patients give a wrong address or live out of the city and cannot be followed. Others refuse to return, even when visited by the nurse and urged to do so.

Of the 75 doubtful cases during the first 10 months:

28 came only once,
12 came only twice, and
54 in all paid less than 5 visits.

From the 956 cases of pulmonary tuberculosis the following statistics are compiled:

Age.

From	1	to	5	years	4
"	6	"	10	"	14
"	11	"	15	"	31
"	16	"	20	"	151
"	21	"	25	"	178
"	26	"	30	"	149
"	31	"	35	"	126
"	36	"	40	"	101
"	41	"	45	"	71
"	46	"	50	"	54
"	51	"	55	"	35
"	56	"	60	"	22
"	61	"	65	"	8
"	66	"	70	"	2
"	71	"	80	"	2

Age not stated in 8 cases.

Thus:

From 21 to 40 years there are 554 or 58.33% of the cases,
From 16 to 45 years there are 776 or 81.85% of the cases.

Sex and Color.

White males	463
White females	287
Black males	121
Black females	85
Males	61%
Females	39%
Whites	78.5%
Blacks	21.5%

Nationality.

Reference is made to birthplace of the parents. Thus under Germans are those whose parents were German, as well as those of German birth.

Nationality not stated in		49
United States	white	194
	black	206
Germans		159
Russians		90
Irish		61
Poles		21
English		10

Austrians	18
Scotch	5
Greeks	4
Norwegians	5
Mauritian	1
Bavarian	1
Lithuanian	3
Galatian	1
Spaniards	2
Canadians	3
Bohemians	9
Hungarian	1
Sicilian	1
French	1
Italians	4

Mixed Parentage.

United States and German	7
United States and Irish	2
United States and Scotch	1
German and Irish	2
German and French	1
Irish and Italian	1
English and Dutch	1

Of the white patients:

27.7% are of American descent,
21.2% " " German "
12.8% " " Russian "
8.7% " " Irish "
2.5% " " Austrian "

All of the Russians and Austrians are Jewish, giving roughly 15 per cent of the white patients as Jewish.

Condition.

(Figures from the second year only.)

Condition not stated	5
Single	271 = 53.5%
Married	204 = 40.3%
Widowed	31 = 6.1%

Exposure.

FIRST YEAR.

	Cases.
History of unusually intimate exposure	44
History of less intimate exposure	102
History of doubtful exposure	53
No history of exposure obtained	228
No data	18

SECOND YEAR.

	Cases.
Conjugal exposure	20
Intimate association in immediate family	75
Intimate association with patient outside of family	21
Exposure in workshop	28
Incidental exposure	26
No history of exposure obtained	295
No data	46

TOTAL.

History of definite exposure in 41.3%
History of very intimate exposure in 18%
No history of exposure obtained in 58.6%

The more carefully a patient's past history is inquired into the more often a definite history of exposure is obtained. Our histories are taken largely by students and other inexperienced assistants and the figures represent a very conservative and probably even a very low estimate. The following figures from the first year are suggestive:

Cases with a tuberculous family history, without history of exposure	18
Cases with history of exposure, definitely without tuberculous family history	55
Family history insignificant, exposure marked	5

The Initial Symptoms.

Cough	574
Hæmoptysis	72
Influenza or a "cold"	53
General constitutional symptoms, fever, malaise, "run down," etc.	67
Pain in chest	52
Pneumonia	19
Pleurisy	10
Typhoid fever	6
Chills and fever	14
Intestinal disorders	13
Dyspnœa	9
Measles	3
Hoarseness	4
Pertussis	3
Enlarged glands	3
Sore throat	3
Bronchitis	1
Dengue	1
Coryza	1
Rheumatism	1
Palpitation of heart	1
After trauma	1
Not stated	42

62.8% of cases begin with cough,
7.87% " " " " hæmoptysis,
7.3% " " " " constitutional symptoms,
5.7% " " " " pain in chest,
5.7% " " " as influenza,
2.1% " " " " pneumonia.

The Occurrence of Important Symptoms.

Cough present in all cases except 25
Hæmoptysis in 467 cases or 48.85%

Digestion { Good 532 / Impaired 340 } or 39%

Sweats { Profuse 78 / Occasional 468 } or 57.1%

Stage of Disease.

Although Turban's scale was made the standard of comparison, the figures for the second year were compiled by so many different observers that they are not more than roughly accurate. If error has been made, it is in too lenient interpretation. Many cases placed in the first stage belong to the second and many in the second to the third. The figures for the first year were compiled by a single observer and have, I believe, been more justly apportioned.

First stage:	First year,	66	Second year,	154
Second stage:	" "	160	" "	171
Third stage:	" "	214	" "	155
Not stated:	" "	5	" "	31

Condition of Patients on Admission.

The prognosis made at the time of the first examination gives some idea of the condition of the patient on admission.

Good prognosis given: First year, 50; second year, 57; total, 107 = 12 per cent.

Doubtful prognosis given: First year, 56; second year, 58; total, 114 = 12.82 per cent.

Bad prognosis given: First year, 338; second year, 330; total, 668 = 75.1 per cent.

No prognosis given: First year, 1; second year, 66; total, 67.

Duration of Symptoms Before Admission.

FIRST YEAR ONLY.

1 to 3	months,	57	cases,	or 13.5%
3 " 6	"	90	"	" 21.4%
6 " 12	"	80	"	" 19.0%
1 " 2	years,	75	"	" 17.8%
2 " 5	"	68	"	" 16.1%
5 " 10	"	36	"	" 8.5%
Over 10	"	14	"	" 3.3%

Again these figures are valuable only as general indications. As is well known, the more searching our inquiries are the longer the duration of symptoms will appear. Ignorant patients, and particularly colored patients, date their illness only from the beginning of serious symptoms.

Complications.

(First year only, 411 cases.)

TUBERCULOUS.

Laryngitis	27
Bone tuberculosis	6
Pleurisy	8
Ischio-rectal abscess	3
Meningitis	1
Pulmonary fistula	1
Enteritis	2
Otitis media	2
Sinus over sternum	1
Glands in neck	1

NON-TUBERCULOUS.

Bronchitis and emphysema	9
Pregnancy	6
Mitral insufficiency	1
Aortic insufficiency	0
Laryngitis	1
Insanity	1
Bronchitis	1
Syphilis	4
Herpes zoster	1
Arteriosclerosis	4
Alcoholism	2
Hiccough	1
Hernia	3
Gonorrhœal exostoses	1
Gout	1

Probably many complications have been omitted. Where a large number of men are engaged in making records, many details are sure to be overlooked.

Results.

The patients being regularly visited by the nurses has given us unusual facilities for following them. The results in all cases, whether sent to a sanitorium or remaining at home under good or bad surroundings, are given below. Only so small a proportion entered institutions, however, that the number is practically negligible. The results are given up to May 1, 1907.

I. Cases followed for from 20 to 26 months:

Number of cases of pulmonary tuberculosis in first six months		263
Patients living out of city or lost		63
Number of patients followed	200	
Of these are dead	119	or 59.5%
Of these are living	81	or 40.5%

Of the 81 living: 31 are improved, 27 remain unchanged, 23 are worse.

II. Cases followed for from 14 to 20 months:

Number of cases of pulmonary tuberculosis in second six months		182
Patients living out of city or lost		63
Number of patients followed	119	
Of these are dead	62	or 52.2%
Of these are living	57	or 47.8%

Of the 57 living: 17 are improved, 10 unchanged, 30 are worse.

III. Cases followed for from 8 to 14 months:

Number of cases of pulmonary tuberculosis in third six months		258
Patients living out of city or lost		79
Number of patients followed	179	
Of these are dead	74	
Of these are living	105	

Of the 105 living: 34 are improved, 34 remain the same, 37 are worse.

Totals.—Of 498 cases of pulmonary tuberculosis followed for from 8 to 26 months:

82 are improved	16.4%
71 remain unchanged	14.3%
90 are worse	18.0%
255 are dead	51.2%

Note.—Since this paper was prepared, Mr. Henry Phipps has once more given proof of his broadminded generosity in a gift to us of $1250; $1000 to be used for laboratory work and $250 for the library in the purchase of books and journals on and relating to the subject of tuberculosis. We have been unable heretofore, from lack of funds, to do all the work which we have been eager to do, but shall now be able to carry on investigations which we hope may lead to definite results in the relief and cure of patients suffering from tuberculosis. No class of patients deserves more attention, and to Mr. Phipps, more than to any other American citizen, thanks are due from all, both doctors and laity, for the assistance he has given both here and elsewhere in the relief of these sufferers. It is to be hoped that his example will be followed by others, for there is no more important public work to be done to-day anywhere in the world than to gain control of this disease, which causes a greater loss in lives and money than any other human affliction. We desire, therefore, to express thus publicly our most sincere thanks to Mr. Phipps for his help, and our hopes that in one of his laboratories the long-sought-for cure may be found.—Editor.

THE HOME FACTOR IN TUBERCULOSIS.

A STUDY OF TUBERCULOUS FAMILIES.

By H. H. Hazen, M. D.

There has long been great diversity of opinion as to the part played by heredity in the transmission of pulmonary tuberculosis. As early as 1878 Holden questioned 500 physicians of the United States as to their views upon the inheritability of consumption. In most of the countries of Europe similar investigations were made, but all this work led to no exact results. It brought out merely the divergence in the opinions of medical men. However, a number of investigators were led to careful study of the families with which they came in contact. Lendet and Riffel from their studies came to the conclusion that inheritance played an important rôle in this disease, and to this cause they attributed over 50 per cent of their cases.

Let us now turn to the present views. Baumgarten believes that the disease is transmitted directly from parent to child, either through the sperm, ovum, or placenta, and his adherents call attention to hereditary syphilis and pebrine, so carefully studied by Pasteur, as proofs of the possibility of this manner of infection. Others, as Ogilvie, for instance, believe that the predisposition alone is inherited. They divide this predisposition into two forms, general and local. As an example of the local type Ogilvie claims that the same lung is affected in the child as in the parent. Von Behring thinks that the disease is acquired in early life through the digestive canal and remains latent for perhaps many years, until some favoring circumstance lights up an infection.

At the Phipps Dispensary our feeling is that inheritance plays a very minor rôle, and because of our facilities for the careful study of the home life of our patients, we undertook a careful search into the number of infections occurring in households. Thanks to our Phipps nurse, Miss Spicer, and the two tuberculosis nurses, Miss La Motte and Miss Bond, we have an admirable means to study the home conditions. The family is under a trained eye. Doubtful cases are either sent to the dispensary or examined at home. The material for this paper has been gathered through the painstaking care of these three nurses. Only those families are reported which have one or more members visiting the Phipps Dispensary.

We have studied 83 families, containing a total of 534 individuals. Of these 254, or 47 per cent, are definitely tuberculous, 13 are suspicious, and only 267 are well. At first glance this might seem to speak for heredity, but a moment's thought will show that the intimate contact with members of one's own family furnishes the best possible chance for contagion.

In 48 instances we find at least one child and one or both of the parents infected. Of these cases both parents are infected in 10 instances; the father alone in 12, and the mother alone in 26. The fact that we find mother and child infected more frequently than we do the father and child is easily explained by the necessarily closer contact with the mother. Again, these figures seem to speak for heredity, but let us examine a little further. In three instances in the above series the child developed the disease well in advance of the parent. In 17 instances we find one or more children infected and both parents entirely free from the disease. Out of our total of 254 cases we find 158, or 62 per cent, free from an hereditary taint. The objection may be made that the history was inaccurate; and we must admit that in spite of our utmost care we may have been misled.

Is there the possibility of contagion between individuals who are in as intimate contact as in family life, and in whom hereditary transmission from a common source can be ruled out? We naturally turn to man and wife. What do our figures show? We find 21 instances of conjugal infection, and two instances in which one party has it and the consort is suspicious, and only 25 instances in which one partner has tuberculosis and the other is living and well. That is a most remarkable record. It well illustrates the danger of prolonged intimate contact. And I wish to emphasize the fact that in every case the family history of the consort who last develops the disease is negative. Among our dispensary cases we have several records similar to Weber's, where one man has the disease himself and has lost two or more wives from the same cause; but among the 83 families studied there are no such cases. While speaking of conjugal infections, I must mention a recent report by Weinberg. He has studied the surviving consort in 4000 patients who have died of tuberculosis, and finds that their death rate is just twice as high as that for other widows and widowers. The percentage of infection from husband to wife, or vice versa, is not quite so high as that from mother to child, but is very high, nearly one-half of our married patients having infected their consorts. In two-thirds of our cases a diseased parent has infected one or more children. Of 48 individuals who were exposed by marriage, 21 have contracted the disease and two are suspicious. I have already mentioned that in 48 instances where there was a diseased parent, one or more children developed the disease. In these 48 families there are 237 children, and of these only 92 developed tuberculosis, while five are suspicious. In other words, where one consort had tuberculosis the other developed it in 43 per cent of the cases; whereas of those exposed to parental infection, only 38 per cent developed it.

In 15 instances one or both parents have pulmonary trouble and the children are entirely well.

Of distant relations who have spent some short time with the family, we find but three infected,—a rather small percentage if we consider the family tainted.

In five instances a person coming from a sound family has married into a tuberculous family, the consort not being

diseased, and has developed the disease. Five may not seem a large figure, but it constitutes nearly two per cent of our cases.

And now comes a most important fact. Only three out of 254 members a trifle over one per cent of these 83 tuberculous families, who were not in contact with their families, developed the disease. If we accepted heredity as the most important factor we should look for a larger percentage.

Excluding conjugal infections, we have 11 instances where an individual moved into a house in which lived, or had recently lived, tuberculous patients and developed the disease.

To sum up: In 62 per cent of our cases there is no tuberculosis in the immediate ancestors. Forty-three per cent of those exposed to marital infection became infected; while only 38 per cent of those exposed to parental infection developed the disease. Only three individuals of tuberculous stock developed lung trouble when not in association with their families. There are 11 well-marked instances of house infection. In view of these facts, I cannot help believing that infection acquired by long continued and intimate association plays the only rôle in the transmission of pulmonary tuberculosis. Findel, in Flügge's laboratory, has shown that to certainly infect a guinea pig it must be made to inhale at least 90 tubercle bacilli. A few bacilli have no effect. This is good experimental evidence that to produce pulmonary infection a large number of bacilli must be taken into the respiratory tract. If true of the guinea pig, this is probably true of man, and one can readily see that the liability to develop the disease after incidental contact is but slight.

In conclusion I add the history of one remarkable negro family in which the disease ran through four generations. In order to confirm the diagnoses, I personally examined the family. Millie, the great grandmother, has a healed lesion in her left upper lobe. She had ten children, two are well, one (Kate) is suspicious, and the other seven definitely tuberculous. Kate had three children, two are well, but the third (Irena) is tuberculous. Irena's four children are all afflicted. A total of 13 positive and one suspicious case in one family, all having at some time lived together.

Note.—These very striking figures, important and illustrative as they are, cannot be applied without reservation to the whole of our material. The 83 families referred to were selected for study on account of the large number of infections which had occurred in each, and on account of the favorable conditions for observation.—L. H.

THE EARLY DIAGNOSIS OF PULMONARY TUBERCULOSIS.

By Louis Hamman, M. D. and Samuel Wolman, M. D.

Early cases of pulmonary tuberculosis may be regarded hopefully from the point of view of cure, but the multiform character of the disease, and its grave course in some instances, make it absolutely necessary for us to diagnose each case as soon as possible, so that a systematic, vigorous, and efficient treatment may be begun in time. While some cases recover without treatment, and others respond readily to treatment, many, although diagnosed in the early stages, cause great anxiety to their physicians, and may even end fatally in spite of the best of care. Therefore, the earlier a diagnosis is made is of the utmost importance, not only to the individual concerned, but to all who are directly or indirectly associated with him. On account, however, of the necessary changes that must be made in the patient's life, many doctors are reluctant to pronounce sentence as it were, unless there is present marked evidence of the disease. We are convinced, on the other hand, that even the slightest changes in the normal physical signs are important, and the records of our Phipps Dispensary have been searched with a view to determine how slight may be the signs and symptoms which may justify one in making at least a tentative diagnosis, and in subjecting the patient to close observation or to the tuberculin test.

After studying the 1745 histories taken in the Phipps Dispensary during the first two years of its work, we find that about 150 may be classed as early. A large number of these may be accurately classed as tuberculosis from the physical signs alone. They all show definite though slight changes in percussion note, modified breath sounds, and the presence of râles. We shall not discuss cases presenting these three physical signs, since there should be no longer any doubt as to the diagnostic value of this combination of signs. There remains, nevertheless, a group of cases in which these three signs were not always associated. All the patients in this group were proved to have pulmonary tuberculosis, either by the presence of tubercle bacilli in the sputum, or by the tuberculin reaction, or by the further course of the disease with the development of a more advanced lesion with definite and indisputable physical signs, the lesion being located at the site where the suspicious signs were found during the early examination.

Sixty-one patients by these means, where the physical examination was not alone sufficient to prove the existence of the disease, were proven to have pulmonary tuberculosis. In some of these patients there was an altered percussion note, in some modification of the breath sounds, in some râles. In many only one of these signs was present; in some but two of them. In none were all three found.

A change of the percussion note was detected in 29 of the 61 patients, or 47 per cent. Râles were heard in 53 per cent. The breath sounds were modified in 61 per cent. In round numbers, then, we may say that 50 per cent represents the frequency of occurrence of any one of the three signs in early cases. It is interesting to note that in fully one-third of these incipient cases, only one of the three signs was present; a changed note in 5 per cent; modified breath sounds in 13 per cent; râles in 15 per cent. The altered percussion note

was sometimes hardly perceptible; the modified breath sound in some instances was only a roughening of the inspiration; and the râles in many instances were indicated by a barely perceptible crackling; in a few but a single click was heard.

In nearly two-thirds of the group a combination of *two* of the above mentioned physical abnormalities were present, the distribution being as follows: altered percussion and râles in 16 per cent; modified breath sounds and râles in 23 per cent; changes in percussion note and breath sounds in 25 per cent. The most frequent combination is that of modified breath sounds with either of the other two signs. Râles, however, form the most frequent single sign.[1]

Tubercle bacilli were found in the sputa of 24 out of these 61 cases, or 39 per cent. A positive tuberculin reaction was obtained in 24 other cases that did not show bacilli in the sputum. In the remaining 13 cases, the progress of the signs leaves no doubt as to the diagnosis.

A surprisingly large number of these patients presented themselves with cough and sputum, 89 and 87 per cent respectively. In 66 per cent the respiratory rate was above 20. Forty-two per cent complained of a loss in weight, but fully half of these knew of no disturbance in digestion or appetite to account for the loss. Chills, sweats, loss of appetite, and impaired digestion occurred less frequently. It was impossible to obtain continuous temperature records of these ambulant patients.

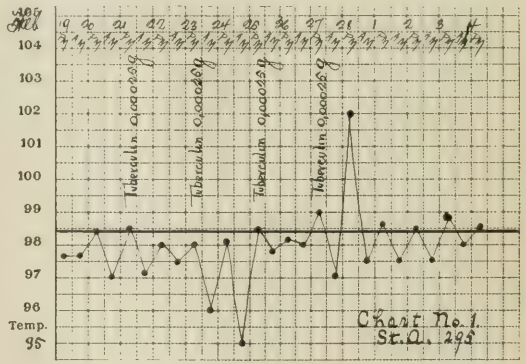
Considering the very early stage of the disease in these patients there is an unexpectedly large occurrence of hæmoptysis—56 per cent; and 16 per cent indicated hæmoptysis as the initial symptom. In order of frequency the initial symptoms are cough, 56 per cent; pain, 22 per cent; hæmoptysis, 16 per cent. A few gave weakness or loss of weight as the primary symptom. It is probable that hæmoptysis is not as often the initial symptom as our figures indicate; for the spitting of blood hurries the patient to the doctor much sooner than other symptoms which appear less grave to the patient. In two cases the lungs were apparently clear, but both had had hæmoptysis and both reacted to tuberculin.

Symptoms are of undoubted importance in the diagnosis of early cases, but not of as much as the signs, except of course that it is the symptom and not the sign that brings the patient to the doctor. We have seen a considerable number of patients without symptoms, who were discovered during the routine examination of the members of families in which there were one or more tuberculous patients. This experience shows how many more patients suffer from this disease than is commonly supposed. Even with all these symptoms, with the exception perhaps of hæmoptysis, the finding of such slight signs does not actually prove the existence of pulmonary tuberculosis.

[1] By a changed note is meant not only an imperfect but also a hyperresonant note; by modified breath sounds, not simply an intensification or prolongation, but also a suppression of them. Our records show diminished movements of the chest at the site of the lesion in more than one-half of the incipient cases, but as this sign is in these cases often difficult to appreciate, we do not lay stress upon it.

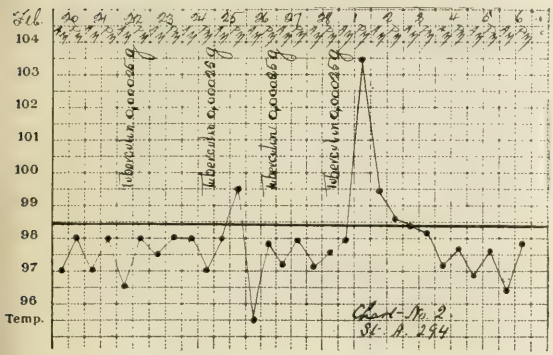
Further observation of the patient's temperature, pulse, weight, and other clinical symptoms and repeated examinations undertaken preferably at different times of the day, with more than one careful sputum examination, are demanded. After all this the diagnosis may still remain in doubt, and it is in this group of cases that tuberculin has rendered an invaluable service. Tuberculin must, however, be used intelligently. When it is used with care there is no danger to the patient, but it is in the interpretation of the results that caution is necessary. Its specificity has been determined beyond doubt, and the only just objection to its use in diagnosis is that the reagent is too delicate and may give a reaction which is easily to be interpreted falsely. It is well to recall the figures of Franz, who injected 400 recruits of the Bohemian army, able-bodied, apparently healthy men, and found that 61 per cent (!) reacted. It is only when the tuberculin reaction is viewed as a part of the whole clinical picture that it acquires importance.

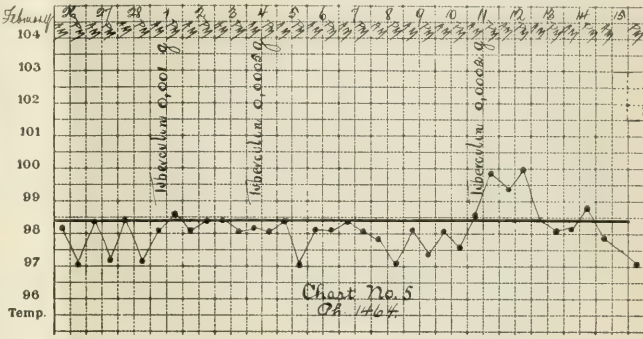
The original directions of Koch to use one, five, and ten milligrammes, and repeat the last injection if no reaction occurs, have recently been interestingly modified. Loewenstein suggested using much smaller doses, a fifth of a milligramme and repeating this same dose four or five times. The principle depends upon the assumption that the tuberculin reaction is due not so much to the dose employed as to the hypersensitiveness developed by the injection of repeated small doses. This principle has become established for the albumoses (?) as a class, and is a well-known phenomenon of serum injections. An animal is often killed by the repetition of a dose which on the first injection was harmless. Charts Nos. 1, 2, 3, and 4 show the typical reactions after repeated

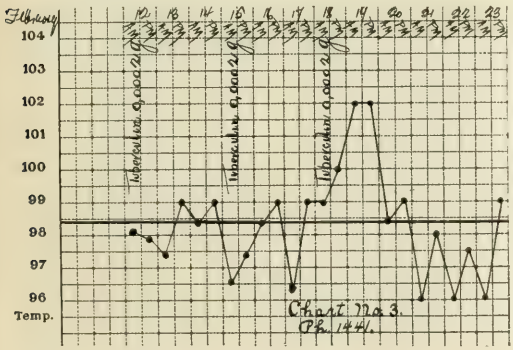


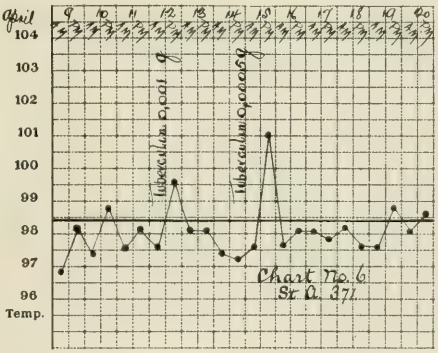
injections of the same small dose. If the principle is true, one would expect a reaction with descending doses of tuberculin, and such reactions do occur. In Chart No. 5 the patient reacted to the third injection, one, one-half, and one-fifth of a milligramme being given. In Chart No. 6 there is a very slight reaction to one milligramme, a most decided reaction to the second dose of one-half a milligramme. These charts emphasize very strongly a caution which was given by Koch

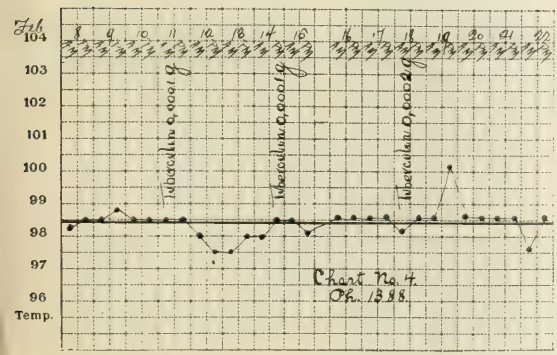
himself, namely, if a patient shows ever so slight a tendency to react to a given dose of tuberculin, the same dose must be repeated before a larger amount is given. Attention to this caution will prevent many unpleasant results. The advantages that may be claimed for Loewenstein's method are that the reaction is milder, and, therefore, its dangers are minimized and that not as many obscure but unimportant (healed?) tuberculous foci are revealed as by the larger doses. The objections to the method are that many cases that fail to react to the small doses do react when larger doses are given, and if we restrict ourselves to a fifth of a milligramme, many cases of tuberculosis will pass undetected and the whole value of the method be compromised. Bandelier and Rolpke particularly emphasize this

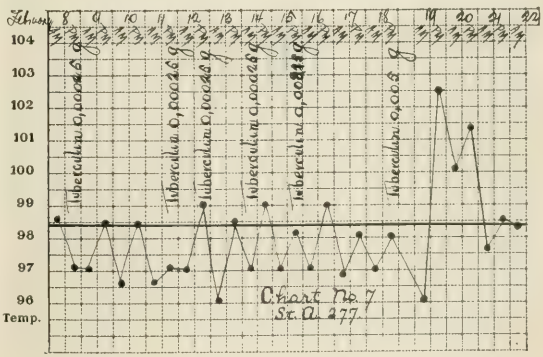






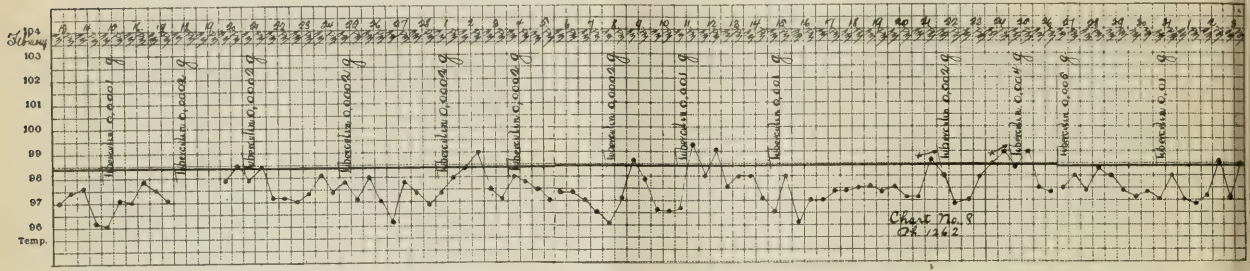


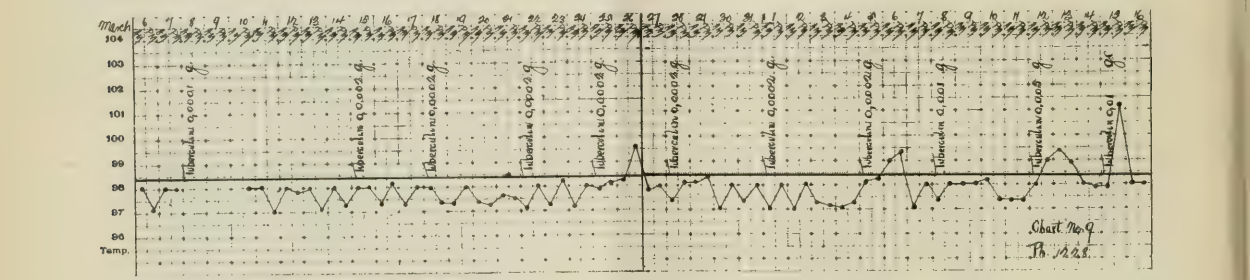




point; which from the report of their cases seems well justified. Chart No. 7 shows a marked reaction to five milligrammes after repeated injections of a quarter of a milligramme were unavailing. Although repeated small doses do develop a hypersensitiveness, it is well known that if

great obstacles in the way of a correct interpretation. We have no special formula to suggest, but we feel that to repeat a fifth of a milligramme dose three or four times and then ascend rapidly to larger doses, as one, five, and ten milligrammes is a particularly safe method in ambulant cases.

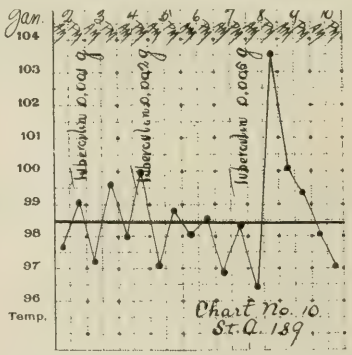




repeated frequently enough, an immunity is developed, and by giving too many small doses we may render the patient insensitive to larger doses. Several of our charts offer this suggestion, but of course the interpretation is uncertain. In Chart No. 8, after a very slight reaction to the small dose, no further reaction appears, even when ten milligrammes is given. In Chart No. 9, after several very mild reactions, there is no further reaction until ten milligrammes is given. The third objection to the method is that it is time-consuming, which of course is invalid if it is proven that it has any decided advantages.

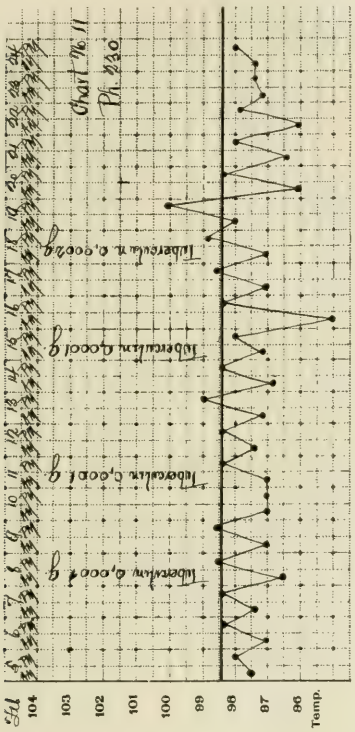
Another much discussed point is the maximum dose. Is it necessary to give as much as ten milligrammes, or wise to repeat this dose, as Koch advises? Bandelier in a very exhaustive article, insists most strongly upon following accurately Koch's directions. Certainly we have by the old method obtained reactions to ten milligrammes in cases where there could be little doubt of the presence of tuberculosis. In one instance particularly, where the patient did not react until the second ten milligrammes was given, the diagnosis was later confirmed by the appearance of hæmoptysis. Whether such high doses are necessary when preceded by repeated small doses, is questionable. As we have said, it is a disadvantage to have the reaction too fine, but the whole question needs longer and more systematic study. Unfortunately, there are

In the interpretation of a tuberculin reaction three factors must be considered,—the temperature, the constitutional symptoms, and the physical signs. These occur without any definite relation to one another. In Chart No. 10 the temperature is



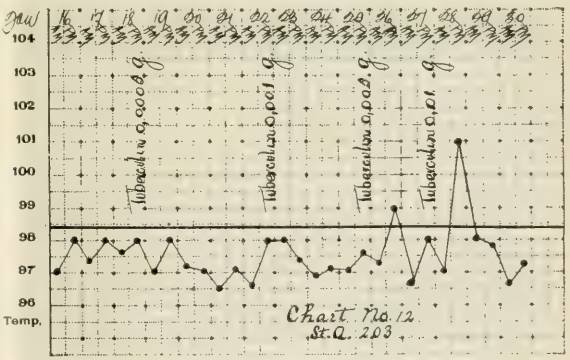
recorded as high as 103 degrees, while the patient has scarcely any constitutional symptoms. In Charts Nos. 4 and 11 the temperature was below 100 degrees and the constitutional symptoms were intense. The third feature, the physical signs of the reaction, is by far the most important, for we then not only know that the patient has an active tuberculous lesion,

but where it is and something about its extent. Although a local reaction must always occur, unfortunately the lesion is seldom so favorably placed that we can detect it. Rolpke reports obtaining signs of local reaction in 45 per cent of his



cases, but this is an exceptionally high percentage. In 30 of our cases unequivocal changes in the local signs were observed in only six.

To summarize then, we may say that a negative reaction is positive information, and information which is often extremely valuable. We recall particularly, one instance in which the symptoms and physical signs were so very suggestive that without tuberculin we should certainly have made a definite diagnosis to avoid the possibility of falling into a graver error. When together with the general and the febrile reaction, there are definite signs of a local reaction, the test is one of the most satisfactory and convincing of all our diagnostic methods. A large group of cases remains, which react positively, where a great deal of care and judgment must be used in our interpretation. It must be remembered that a patient may have a pulmonary disease other than tuberculosis and still react to tuberculin. For instance, Chart No. 12 shows a typical reaction to ten after one-half, one, two, and five milligrammes had been given. The clinical history, the physical examination and the sputum examination make the diagnosis of bronchiectasis almost certain, and while it is safe to assume that the patient has either a glandular or a pulmonary tuberculous lesion, we feel confident that tuberculosis is not the disease causing the symptoms. The tuberculin reaction can in no way replace a careful and painstaking examination, for it is just in those instances, where, after repeated examinations, we have found suggestive signs, that tuberculin finds its most valuable application. It is another bit of evidence added to the history and the examination, and is only of importance when viewed in the light of these. We are willing to admit that relying upon its aid we may send to the sanitorium some patients who would have perfectly recovered had they continued their accustomed mode of living, but no one can say which case of tuberculosis will be arrested naturally, or which one will progress if untreated. It is to-day almost universally acknowledged that the cure of pulmonary tuberculosis has been grossly exaggerated and our only hope for satisfactory results is in the treatment of just such early cases. We feel very strongly that we have done our best duty, even if we condemn needlessly one patient to a year of treatment, if by doing so,



we with certainty completely restore three, or only two, others to perfect health.

In conclusion we desire to express our opinion that in the diagnosis of an early case of pulmonary tuberculosis no abnormality of the physical signs should be disregarded, no matter how unimportant it may appear at first sight. A single click, if it persists after coughing and deep breathing, and especially if it is heard at the same spot on subsequent examinations, should put us on our guard, and arouse us to use all the means we have to make a correct diagnosis—whose importance is inestimable in these cases. Only in this way will it be possible to diminish the enormous mortality and morbidity which accompany this disease, and which are a disgrace to the medical profession, who to-day, more than ever before, are responsible in large measure for the conditions of life resulting from tuberculosis.

THE CRUSADE AGAINST TUBERCULOSIS.[1]

By Lawrence F. Flick, M. D.

From the dawn of history consumption has been the giant foe of mankind, paralyzing all resistance by the majesty of his havoc. Here and there seers of medicine read aright his pedigree and hinted at methods by which he could be exterminated, but their prophecies fell upon dead ears. Not until Pasteur and his followers gave the world the 'magna charta' of emancipation from superstition was his doom forecast; and when Koch discovered the tubercle bacillus in 1882, science wrote his death warrant. Before that time civilization had struggled in vain against the monster.

Since Koch's great discovery wonderful strides have been made in the campaign against tuberculosis. The warfare began with the cry of the forerunners, who shouted the new gospel from the house tops, but as men crying out in the wilderness. They were teaching new and strange doctrine so at variance with accepted views that the world sneered at them as false prophets and decried them as crazed fanatics. So full of hope, however, was the new doctrine and so well embossed with the image of truth that it attracted attention and gradually won the minds and hearts of men and women all over the world. Here and there neophites gathered together, joined forces and pledged themselves to work in unison for the conversion of the world. Societies for the prevention of tuberculosis sprung up everywhere and almost in the twinkling of an eye civilization felt the influence of a new force in the crusade against tuberculosis.

Nowhere in the history of civilization can we find a movement for the betterment of mankind springing into existence so quickly and unostentatiously as has this crusade against tuberculosis. Not with the herald of music nor with the clatter of arms has it come, but with the silence of the recluse; not by the sword at the command of kings, but by the pen of the scientist and alms of the philanthropist. With the force of truth the new word has penetrated the multitude and has borne fruit in action for the amelioration of the sufferings of the consumptive and for the prevention of the disease which afflicts him. Without knowing the why and the wherefore, men and women have been transformed over night from rabid opponents of the new doctrine into ardent advocates of it and in the ardor of their new faith have vied with one another for the accomplishment of practical results. Poor and rich alike are contributing everywhere to the funds for carrying out the work and legislatures the world over are spending money freely for its purposes.

One can scarcely realize that the first society for the prevention of tuberculosis in the world was founded in the city of Philadelphia as recently as April, 1893, when the Pennsylvania Society for the Prevention of Tuberculosis was organized. Almost simultaneously with the organization of this society came that of a similar society in Paris. For a few years these two organizations were alone in the field. The Pennsylvania society sent literature on the prevention of tuberculosis in the form of tracts to all parts of the world; and under the auspices of the French society a journal on tuberculosis was established, which has done much to enlighten the world along scientific lines. Soon societies for the prevention of tuberculosis sprung up everywhere, both in America and in Europe, and wherever they did spring up they attracted the attention and gained the support of intellect and power. With the increase of the number of societies came new journals and new literature of all kinds so that the world was flooded with information upon the subject of tuberculosis from every possible point of view. So extensive has this literature become that it is no longer possible for one individual to keep track of it. Countries, states, cities, towns, and even boroughs now have their local movements, often with their own literature, vieing one with another for the accomplishment of the great purpose of all, the extermination of the great white plague.

Early in the crusade against tuberculosis it was foreseen that some supervision would be necessary to keep the work within proper lines and with this object in view the leaders of the movement in Europe met and organized on international lines. In 1898 the first gathering of this kind was convened in Paris in the form of a congress. Men from different parts of the world met and interchanged thought. A second meeting was held in Berlin in 1899, a third in Naples in 1900, a fourth in London in 1901, and a fifth in Paris in 1905. All of these meetings were called congresses, and while strictly national in organization up to that of 1905, which was international in organization, all were more or less international in character. As a rule they were held under the auspices of the government of the country in which they convened and bore the reputation of official gatherings. Much was accomplished in education at these meetings and the delegates who attended them returned to their homes consecrated with new force and endowed with new energy for the campaign in which they had enlisted.

At the meeting in Naples in 1900, a Central International Bureau for the prevention of consumption was organized with headquarters in Berlin. This bureau is made up of representatives from national associations for the prevention of tuberculosis and constitutes a sort of international society for the prevention of tuberculosis. It held its first conference in 1902 in Berlin, its second in 1903 in Paris, its third in 1904 in Copenhagen, its fourth in 1905 in Paris, its fifth in 1906 at The Hague, and it is scheduled to hold conferences in some part of the world every year. At these conferences papers on the subject of tuberculosis are discussed by scientific men and philanthropists, plans for the prevention of tuberculosis are compared and new plans formulated.

At the Congress on Tuberculosis which convened in London

[1] Read before the Third Maryland State Conference of Charities and Correction, April 26, 1907, McCoy Hall, Baltimore.

in 1901 under the auspices of the English Society for the Prevention of Tuberculosis and the patronage of the King of England, the Royal Family, and the English government, it was decided to make future congresses international in character and in form. An invitation was accepted from the French government to hold the next meeting in Paris in 1904 with the understanding that all governments of the world would be invited to participate through official delegates. Subsequently the date of meeting was changed from 1904 to 1905, and the fifth congress on tuberculosis, being the first strictly international congress, was held in Paris from October 2 to October 7, 1905.

In our own country a successful effort to unify the local movements and co-ordinate them was launched in Baltimore in 1904. The seed was sown at the first tuberculosis exhibition in Baltimore and germinated at a meeting held under the auspices of the Henry Phipps Institute in Philadelphia to hear the paper of Maragliano in March, 1904. The little plant was set in stronger soil at a meeting called for that purpose at Atlantic City in May, 1904. At this meeting the destiny of the crusade against tuberculosis in the United States was finally fixed and a threatened danger of having this grand movement fall into the hands of charlatans was obviated. The National Association for the Study and Prevention of Tuberculosis was organized, and that organization has held two successful meetings in Washington since, one in 1905 and one in 1906. The two volumes of transactions of the society tell forcibly what the society has accomplished since its organization.

The International Congress on Tuberculosis in Paris in 1905 was a great success. Workers in the crusade against tuberculosis convened from all parts of the world, some as the official representatives of the countries from which they came and others as volunteers in the great army of the crusade. Between four and five thousand people registered as adherents of this congress, and whether they came as official delegates or as privates in the ranks, all brought the fruits of their labors and offered them freely on the altar of the common cause. From the North and from the South and from the East and from the West came the wise men and the patriarchs all burning with zeal for the great work upon which they had embarked, and they departed from thence at the end of the congress filled with enthusiasm and burdened with new ideas.

The exhibit at the Parisian congress was a revelation to all who saw it. It demonstrated that the whole world is alive to the importance of the crusade against tuberculosis. From all parts objective displays were made of work done and of the manner in which it is done. There were bacteriological and pathological exhibits which gave a most complete demonstration of the ravages of tuberculosis throughout the animal kingdom and of the manner in which the tubercle bacillus operates to the detriment of mankind. There were carefully prepared statistics showing the damage done by tuberculosis in the past and in the present and exemplifying the benefits accruing from the crusade against the disease. There were exhibits of institutions which have been erected in various parts of the world for treating consumptives in all stages of the disease; of object lessons on sanitation in the interest of the crusade against tuberculosis for practically every department of life, so arranged that they could be studied comparatively; and of mechanical appliances and instruments which are used in one way or another in dealing with the tuberculosis problem in its many phases. In short the exhibit was for the scientific and the philanthropic world what commercial exhibits are for the world of trade. It was a world's fair in science and philanthropy and gave the visitor an opportunity of seeing for himself what the crusade against tuberculosis means in its practical application and of comparing the weapons which have been made for the fight in different parts of the world and selecting for himself those which are most suitable to the place in which he is engaged in the campaign.

One of the surprising things at the congress in Paris was the strength of some of the smaller countries in the crusade against tuberculosis as reflected by their exhibits compared with the strength of the crusade in some of the larger countries. To us of the United States, for example, it was a revelation to find that some of the South American countries surpassed us in the practical application of the new doctrines about tuberculosis to every-day life for the modification of customs and habits. Buenos Ayres, of the Argentine Republic, showed work in the crusade against tuberculosis the most advanced of the Western Hemisphere and perhaps of the world. The United States was poorly represented in its work inasmuch as very few of our states and cities presented their work at all, but had our country been represented at its best it could not have competed with Buenos Ayres. Germany probably led the world in its exhibit, as it leads the world in the crusade against tuberculosis.

At this meeting in Paris the congress was invited to come to the United States by our National Association for the Study and Prevention of Tuberculosis, the invitation receiving the personal endorsement of President Roosevelt through Ambassador McCormick. The invitation was accepted and the next session of the congress was fixed for 1908, the place and date being left open for settlement by the National Association. An invitation was extended at the same time to the Central International Bureau for the Prevention of Consumption to meet in the United States at the time of the meeting of the congress and this invitation was likewise accepted. Acceptance of both invitations was not only unanimous but most hearty, foreboding successful meetings for both organizations in the United States.

The National Association has selected Washington as the place of the meeting of the congress; has tentatively fixed the time of meeting between the last week of September and the second week of October, 1908; has adopted general plans for the congress; and has appointed a committee on the congress with full power to act. Preliminary work has been done by this committee and some of the machinery for the congress has already been created. The committee is endeavoring to raise a fund of one hundred thousand dollars from private

sources for the defrayal of expenses of the congress and has thirty thousand dollars of this fund in hand. An office has been opened at 810 Colorado Building, Washington, D. C., and Dr. John S. Fulton, of Baltimore, has been installed as secretary-general of the congress. Dr. Fulton's administrative ability and wide grasp of the general subject of preventive medicine as demonstrated in the past make his selection for the position of secretary-general ominous of success for the congress.

The thirty thousand dollars which has been contributed towards the fund for the congress has been given by six philanthropic men, each of whom has given five thousand dollars. It is believed that fourteen other far-seeing, public-spirited citizens can be found to contribute the balance of the fund. Those who have given, have given with a promptness and heartiness most encouraging and most inspiring. This example will undoubtedly be followed when the subject has been properly brought before the public. Millions of dollars have been contributed in the past by far-seeing citizens for the advancement of commercialism through fairs and exhibits, and the claims which an enterprise of this kind makes upon a man of wealth so far surpass the claims of mere commercialism that one cannot doubt the willingness of men to support such an enterprise. Men who can afford to give need but be informed of what the undertaking means to be induced to give lavishly all the money that is needed.

The fund of one hundred thousand dollars which is to be raised from private sources is to be used for the advancement of the scientific and philanthropic part of the congress only. Expenses for the entertainment of delegates are to be met in other ways. If the congress is to be put on as high a plane as is contemplated by the committee, it will take all of the hundred thousand dollars for the scientific and philanthropic part of the work. A course of thirty lectures by the most prominent workers in the tuberculosis cause throughout the world outside of the United States is to be provided for out of this fund with honoraria to the lecturers commensurate with their dignity. Other expenses to come out of the fund will be those for the creation of machinery for the congress; for buildings necessary for the exhibit; expressage on foreign exhibits both ways; installment and removal of exhibits; supervision and care of exhibits while the congress is in operation; the equipment and direction of the congress while in session with all clerical, page and janitor forces necessary; printing, stationery, and postage for the preliminary work of the congress and for the congress itself; translating, editing, and distributing the transactions of the congress; and official expenses of the secretary-general with all the clerical force necessary for his work during a period of nearly two years.

Steps have already been taken by the committee on the international congress to secure the co-operation of the United States government and of the various State governments. The secretary-general has done much preliminary work in this regard and the prospects of having the co-operation of our governments are very good. The United States and the various States of our Union will be expected to make appropriations to cover the expenses of their own exhibits and of their participation. All foreign governments will likewise be invited to participate, and most of them, no doubt, will defray the expenses of their own exhibits. The congress, however, will have to stand prepared to meet such expenses as will not be met by invited guests who participate in the congress. So far everything has been planned on a broad basis with a view of giving an impetus to the crusade against tuberculosis in this country and throughout the world. For the purpose of promoting activity prizes will be offered in various fields of work in the crusade to be awarded during the congress. One such prize has been announced, and others will be announced in the near future.

Since the organization of the National Association for the Study and Prevention of Tuberculosis in 1904, great progress in the crusade has been made in the United States. Societies for the study and prevention of tuberculosis and for the establishment and maintenance of sanatoria have sprung up everywhere. In many states, hospitals, sanatoria, and dispensaries either have been established or are under construction. Some of the larger cities have made provision for their consumptive poor and others have the subject of making such provision under advisement. There is activity everywhere and most of it is well directed. We are perhaps not as well organized as some of the European countries, especially Germany and France, but our movement is a live one and contains all the elements of success. In some things our work surpasses that of any other country, and there is reason to believe that if we will organize ourselves a little better and bring our work under a little better control we can confidently enter the race for the extermination of tuberculosis with fair prospects of winning out.

In the matter of general education on the subject of tuberculosis and of the application of modern knowledge for the treatment of tuberculosis the United States probably surpasses any country in the world. The American people are a reading people and newspapers have done much in helping spread the modern knowledge about tuberculosis. We also are a very practical people, and the new knowledge has been applied in the treatment of tuberculosis exceedingly well. Our educational methods, however, have not been without pernicious influence. Teaching the people at large through the newspapers is a quick way of educating them, but it is inaccurate and often leads to error and false impressions. In some regards the pendulum has swung too far and our people have been thrown into consternation by exaggerated views. This is particularly true of the contagiousness of tuberculosis. We have not yet recovered from the shock of discovering consumption to be a communicable disease and the majority of our people are still suffering from the hysteria into which it has thrown them.

One of the most urgent needs of the hour in the crusade against tuberculosis is reassurance of the public in the matter of danger from tuberculosis. We must educate the people about the true nature of the contagiousness of tuberculosis, but upon correct principles. Consumption is a contagious disease in that it is implanted by contact with a person who

has the disease or with a place or thing which has been in contact with a person who has the disease; but contact can be made harmless through the intelligence of the parties concerned. Moreover, not only is contact with person, place or thing necessary, but that contact must be prolonged, intimate and by a person with some susceptibility. Mere casual, temporary contact under proper sanitary environment does not give an implantation. The medium of contagion of tuberculosis is gross in character, easily seen and easily controlled, and for this reason the contagiousness of the disease can be obviated by intelligent co-operation between the person who has the disease and the person who is in contact with him. The contagiousness of tuberculosis exists, but can be nullified by the observation of simple rules. For practical purposes consumption can be made noncontagious, and a full knowledge of this fact by the public at large will quiet all fear.

There probably is no more important task before us at the present stage of the crusade against tuberculosis than teaching every man, woman, and child the methods by which a consumptive can be made harmless to others. There are various methods, all of which have for their object the destruction of the tubercle bacilli given off by an infected person before they can be implanted in another. Methods differ somewhat, consistent with efficiency, but the principle underlying all is the same. The simpler and more economical the method the better, if for no other reason than that of universality of application. When all follow the same practices there is less likelihood of misunderstanding and dissatisfaction.

Perhaps the simplest and most economical method so far introduced is: To deposit all sputum, when the lungs are affected into a paper sputum cup which can be held close to the mouth; to wipe the mouth carefully after each expectoration with a paper napkin, fold up the paper napkin and deposit it in a paper bag; to hold a paper napkin before the mouth when coughing, fold up the paper napkin and deposit in a paper bag; burn the paper sputum cup, disinfect the metal holder of the sputum cup, if a metal cup has been used, by boiling, and burn the paper bags containing the napkins; and when the broken down tuberculous tissue is given off from some other part of the body than the lungs to carefully gather it up with absorbent cotton, deposit it with the cotton in a paper bag and promptly burn the bag and contents. Disposal of sputum or broken-down tissue must be prompt, exact and without contamination of anything. If possible, all sputum should be burned and all things which have been contaminated by it should likewise be burned, but if this cannot be done it should be sterilized with a germicide powerful enough to do this and all things which have been contaminated should be sterilized. Before sterilization the sputum should be completely macerated with lye or some strong alkali capable of macerating it. Men who expectorate should not wear beards and above all should not wear mustaches. Everyone who has to do with expectoration either in giving it off or in handling it should be extremely careful not to soil the hands. All people who expectorate should at all times carry with them the material necessary for proper disposal of sputum. Men should carry paper pocket sputum cups, paper napkins and paper bags in their pockets, which they can do very conveniently and women should carry them in hand bags.

An item of education of very great importance at the present time is the proper disposal of expectoration of every kind. Our new ideas about disease must be engrafted upon our social customs. People must be taught to look favorably and approvingly upon practices for the prevention of disease which have to do with spitting. It will be a happy day for civilization when careless expectoration of matter of any kind from the respiratory tract will be placed in the same category as indiscriminate deposit of excreta, which long since has been banished from civilized life. The person who uses a pocket sputum cup for expectoration in public and openly practices measures for the prevention of disease should be looked upon with favor and approval and not with scorn and contemnation. As things now are the consumptive who openly does what is necessary for the protection of others is feared and avoided, while the consumptive who follows practices which endanger everybody about him, but which are in harmony with custom is intimately met and caressed. Of course all of this is due to ignorance and blind reliance upon the past. The use of paper pocket sputum cups for expectoration in public not only by consumptives, but by all who expectorate should be made a social custom, disregard of which is punished by social ostracism. Expectoration is the means of distribution of many other diseases besides tuberculosis and probably has more to do with human ills and human unhappiness than any practice indulged in by man. When the public once realizes this and fully appreciates the protection which an enforced custom of proper disposal of sputum would give, such disposal will be universally established.

Another matter for public education at the present time is the proper disinfection of places and things which have been contaminated with tuberculosis. Could every consumptive be brought under control and made harmless to himself and others, contamination of places and things could not take place and disinfection would be unnecessary. At the present time this is impossible. In fact as society is now organized a relatively small proportion of consumptives are made harmless. There has been a strong opposition to governmental control of consumptives by the medical profession as a body on the plea that the family physician is entirely competent to deal with the problem. The correctness of this plea is not borne out in practice. The family physician gives general instructions about tuberculosis, but does not go into the details necessary for control. I have yet to see the first consumptive who has been brought under discipline, which will make him harmless to others, by the family physician. To tell a man to take care of his spit without telling him exactly how to do it usually means that he spits carefully into a handkerchief, smears his lips and hands with the sputum, soils his clothing with the soiled handkerchief, and contaminates himself and everything about him, or that he spits into some dark place where the sputum is not seen, into a coal scuttle, into the fire in the kitchen, into a spittoon, or on the street, and by any or all of

these methods contaminates his environment as well as himself. No one can spit out without contaminating his own clothing because he is bound to spray some of the sputum upon himself. Instructions which lead to improper practices are worse than no instructions at all, because they carry with them a certain idea of safety and protection which throws people off their guard.

For proper disinfection of places and things contaminated by tuberculosis the first thing necessary is accurate registration. To this men are constantly objecting strenuously for various flimsy reasons, which look strong because they are based upon sentiment and preconceived notions, but which will not bear the light of truth. Now that everybody believes tuberculosis to be contagious, it is absurd to try to hide the person suffering from the disease from the public. If there is danger in tuberculosis, then we should have that danger as open as possible in order that we may protect ourselves against it. Of all things the most to be feared is a hidden foe. It is very probable that much of the unreasonable fear against tuberculosis existing at the present time is due to a general feeling of uneasiness on account of lack of public control. In our free government we mutually agree to permit the government to do that which we as individuals cannot do without trespassing upon the rights of others. In the matter of contagious diseases we realize that we cannot protect ourselves without seriously infringing upon the rights of others, and we cheerfully entrust this whole subject to the government. Did the government know of the whereabouts of every tuberculous subject, and by proper instruction and assistance make every tuberculous subject harmless as, theoretically at least, it can do, there would be no occasion for fear, and the public fear would soon be allayed. The first step necessary for this public control is registration, and agitation for a complete registration of tuberculosis must be kept up until every case has been propely recorded.

With proper registration of tuberculosis disinfection of all places and things which have been contaminated is made possible and should be enforced. Where the government can satisfy itself that practices have been followed which have completely obviated infection, disinfection is unnecessary and need not be insisted upon. Where there is any doubt, however, as to the correctness and efficiency of the practices which have been followed, disinfection of places and things should be carried out by the government or at least under a general supervision of the government by private individuals. Inasmuch as disinfection of places and things which have been contaminated by disease is a very large, extensive project, it might be well for governments to lay down general principles, and in many instances permit individuals to carry out the disinfection upon these principles. In this way every druggist in the land, for instance, might be made an agent of preventive medicine, and a useful field of activity for the druggist might be thus established. No house which has been occupied by a consumptive should be leased to a new tenant without a certificate of health and no thing which has been handled or used by a consumptive should be permitted to be given or sold to another without a certificate of freedom from contamination. If these practices were once introduced their general adoption would become easy. As matters now stand, society has not equipped itself for practical protection against tuberculosis and because of this lack of equipment even those who do understand the subject and are willing to do what is necessary for the protection of themselves and others are unable to carry out the necessary practices in every detail in daily life.

Other subjects bearing upon the prevention of tuberculosis about which the public needs to be educated are ventilation, cleanliness, and sanitary conditions of every kind. The world has made great progress in sanitary science and modern life in large cities has been made possible by reason of this progress. Drainage, sewage, water supply, and heating have been much advanced by modern thought, and the progress along these lines during even the last half century has done much for the prolongation of life and for human happiness and usefulness. Much remains yet to be done even in the vanguard of civilization. Ventilation has not quite kept pace with the other branches of sanitary science, and this is the part of sanitation which most concerns the crusader against tuberculosis. Of all diseases, tuberculosis perhaps more than any other, depends upon contaminated air for its progress. The popular mistaken idea that low temperature is an etiological factor in the production of tuberculosis probably has been and is a serious stumbling block in the way of progress in matters of ventilation. Not only should the public be enlightened upon all of these subjects, but that enlightenment should be made efficient through city ordinances and state laws in building operations, laying out of streets and management of public works. Principles governing the prevention of disease should be incorporated in all new legislation and engrafted upon all old legislation. The protection which the law now gives to the employee and to the individual against bodily injury from physical force should also be given against injury from micro-organisms, setting up pathological conditions in the body when these micro-organisms are spread through carelessness and disregard of sanitary laws. Schools, churches, public places, and institutions of all kinds should be brought under the influence of advanced sanitary science.

Further matters which are of primary interest in the crusade against tuberculosis at the present day are sanatoria, hospitals, dispensaries, convalescent farms, day camps and consumptive colonies. By modern methods of treatment much can be accomplished in the cure of tuberculosis, particularly during the early stages of the disease. Every tuberculous subject who is still in a curable stage should be given an opportunity for recovery, and if his home environments are not such as to make recovery at home possible, provision should be made for his treatment in a sanatorium. Sanatoria, both private and public, should therefore be established all over the country. Many cured consumptives are going into the sanatorium business as a commercial enterprise, and all of these should be encouraged. Sanatoria for people without means should be established by state and city governments

and by private corporations. The public is ready to support such institutions.

For those cases which are advanced beyond recovery, hospital accommodations should be created both for the poor and for the rich. It is difficult to give a dying consumptive all the comforts and alleviation which he is entitled to, with proper protection to others, in the home. In the hospital where everything is arranged and equipped for the advantage of the stricken one, and where every employee is trained to work for the comfort and happiness of that individual all the protection necessary for the well can be given consistently with the greatest amount of comfort and happiness to the afflicted, and without in any way trespassing upon his sensitiveness. For the poor, hospital provision is absolutely necessary in the interest of humanity. As things now are, the poor consumptive ordinarily dies under environments entailing mental and physical suffering which our present day civilization deems unfit for dumb brutes. Moreover, the last few months of the consumptive's life are filled with danger to all those who come under his immediate environment, which can be avoided by removal of the patient into a hospital.

Dispensaries are undoubtedly one of the most potent measures for good in the crusade against tuberculosis at our command. A well conducted dispensary supplies all the conditions necessary for recovery of very early cases of tuberculosis and gives the entrée into the homes of a great many consumptives for efficient educational purposes. Dispensaries can be conducted very economically, at an outlay of not over eight cents per patient per day, and for this reason are available when more expensive measures cannot be afforded. The dispensary might well be made the beginning of the crusade in every community, as it gradually leads up to other more pretentious measures and educates the public for them.

Convalescent farms, day camps, and consumptive colonies can be placed in the same category and are measures which have more to do with the preservation of the health of those who have been restored than with cure and prevention. The average poor consumptive when restored to health is not again able to enter into competition for making a living with people who have never been afflicted with the disease and therefore needs some assistance in his efforts to maintain himself. The convalescent farm is most available and desirable for the patient who has just been discharged from a sanatorium, as it enables him to remain under supervision and direction with an opportunity of earning a little money for a time longer. Day camps are perhaps most adaptable to dispensary patients. The chances of recovery of many dispensary cases could be enhanced by temporary life in day camps, especially such cases as are too far advanced in the disease to follow an occupation. The home environment of such cases is always bad because it is depressing and unsanitary. Consumptive colonies are still on probation, and we are as yet unable to say much about them. They have been tried on a small scale and apparently give satisfaction. Theoretically, there is this to be said in their favor that they give conditions for the pursuit of happiness on the part of those who have been afflicted with tuberculosis which have at least a sympathetic setting and which do not prejudice the interests of those who are thus afflicted.

The crusade against tuberculosis as developed so far, as may well be deduced from what I have already said, is an active campaign in the flush of victory with implements of warfare at hand suitable and well tried. The lines of battle have been drawn, and it is merely a question of soldiers to fight the battle to a finish. The purpose of meetings of this kind is to gather in recruits and send them to the front. Every community now has its recruiting stations, and is doing all in its power to further the campaign. May we not confidently look forward to victory?

THE TUBERCULOSIS SITUATION IN MARYLAND.[1]

By Henry Barton Jacobs, M. D.

In the progress of any movement, it is well from time to time to stop and look about to see where we are, how our work looks in perspective, and then to glance ahead to be sure we are on the right road, what the possibilities for future development are, and in what new direction our endeavors should lie.

The present occasion gives me opportunity for just such reflection upon the tuberculosis movement, a movement for man's relief and betterment which is without a parallel in the world's history in its universality, its enthusiasm, and its hopes, a movement, perhaps, which is bringing the people of the world more closely together in common bonds of interest than any other single force which has ever been inaugurated; for it is a cause which appeals not merely to a few of each country, but rather one which is linked particularly with the interests of the great body of workers of the world, the poor people, wherever gathered together.

We deplore wars, we deplore famine, but, years in and out, neither of these awful agencies is so destructive to the race as is this terrible minute enemy, the germ of tuberculosis, which so silently, so secretively, yet so surely decimates, yes doubly decimates, the population of the world.

But to-night I want to review our work here in Maryland to consider what has been done and what next we need to do. This conference gives me a favored opportunity, for I feel that all who hear my voice are sympathetic and eager to do their part in helping on our cause—not only in influencing the public mind, but also in determining municipal and state legislation.

[1] Read at the Third Maryland Conference of Charities and Correction, April 26, 1907, McCoy Hall, Baltimore.

The position of Maryland in this warfare against tuberculosis is already an enviable one. Not only have we had for years public-spirited citizens who have given their best thoughts, and large donations, to a study of the work, but we have had also two or three successive legislatures and two successive governors displaying a wisdom in the form of laws enacted and approved which in some respects puts Maryland in the very vanguard as regards the state and municipal control of the disease. A short enumeration of the work done by private citizens and a brief reference to these laws now on the statute books will not be out of place.

The very first effort in Maryland to do something for the relief of consumptives was made by a devoted band of men and women some ten years ago, who opened a home exclusively for poor people who should be afflicted with consumption. No charge was made for treatment and no one was expected to pay. This was the beginning of what is now The Hospital for Consumptives of Maryland, with its growing sanatorium at Eudowood. I speak of this institution with a great deal of respect, not only because it was the first institution of its kind in Maryland, but because it was one of the first in the country; perhaps its open-air sanatorium, conducted by private charity exclusively, for the tuberculous poor was the very first in this country. Its beginning was small, but it has now come to be an important factor in the community in offering relief to favorable cases among the indigent.

In the past year, an average of 40 patients per day has been maintained, and 139 different individuals were given care, many of them to return to their homes in renewed health, capable of self-support, and many others in an improved condition, capable of caring for themselves in such a way that they no longer are a menace to their family and friends; while still others were made as comfortable as possible in their journey to and across the dark river of death. But the influence of this sanatorium at Eudowood is not to be measured by the number of patients it has treated, for each one of those who have left it has gone out as a missionary more or less intelligent and active according to his or her capacity. Innumerable friends of patients have visited there, and have seen, whether convinced or not, the manner of complete open-air life, and their testimony cannot but have been and be a force in the right direction.

Coincidently with the progress of the work at Eudowood other creditable factors for relief have appeared in our midst. The Phipps Dispensary of the Johns Hopkins Hospital, founded by the generosity of Mr. Henry Phipps, has for two years been devoting its energies exclusively to aiding poor ambulatory patients afflicted with tuberculosis; over 1500 different individuals have been seen and given such assistance as possible—some to be recommended to Eudowood, others to undertake the open-air life as far as possible in their own home; while all have been advised as to the nature of the disease and how to prevent its spread. This advice and this oversight of patients have been extended to the families of the sufferers through the generosity of Mr. Victor G. Bloede, who has maintained a nurse whose duties were to follow up every patient applying for treatment at this dispensary, and in the patient's home to do whatever willing and sympathetic hands might find to do to relieve conditions there and provide against further transmission of the disease. The amount of good accomplished by this single agency, the dispensary and its nurse, cannot be estimated. A similar dispensary has more recently been established at the University of Maryland, and, within a few months past, another on North avenue.

Maryland has been fortunate in having at the head of its public institutions men of progressive minds eager to take advantage of whatever was new in ameliorating the condition of those under their care. At Sykesville, in the Springfield State Insane Hospital, Dr. Clark has introduced the open-air care of consumptive patients; Dr. Wade has done the same at Spring Grove; and thus these two institutions can be said to be important factors in the elimination of tuberculosis and in exerting an educational influence upon the minds of friends and visitors. It was a source of great satisfaction to learn from an expert in tuberculosis who had recently visited other state institutions that the spirit of the times has impregnated them all and, so far as it was possible for those in charge to arrange it, the victims of consumption in these institutions were segregated from their fellows, other precautions being taken to limit the infection, and all the open air consistent with the condition of the inmates being given to those infected. Whereas ten years ago tuberculosis was the great source of mortality in our insane asylums, prisons, and reformatories, it is now so well controlled that it plays a much less conspicuous rôle. The same, however, cannot be said of all our county almshouses and jails, and to these we must give special attention in the near future.

The dreadful conditions existing but a few years ago in the Bayview Hospital and Insane Asylum have been perceptibly bettered, and now, in the quarters improvised by an ingenious Board of Management, patients from the asylum with tuberculosis may be seen taking the full open-air treatment with wonderful success, considering their mental and physical conditions, and in the almshouse a meritorious attempt is being made to segregate the consumptives and give them the advantage of good food, rest, and open air. Upon the hill adjacent to Bayview there has been erected a ward for the tuberculous poor of both sexes and colors, and, with money for its improvement upon somewhat more approved lines of construction, a most useful nucleus of a municipal hospital for the care of advanced cases of consumption is already at hand.

The laws of Maryland, so far as relates to the State dealing with the tuberculosis problem are eminently satisfactory. We have that most efficient of all laws, which classifies tuberculosis among the infectious diseases and requires all physicians to send notice to the State Board of Health of each new patient seen with tuberculosis in one of its dangerous forms. If this law is obeyed, it makes it possible for the State Board of Health to know the locality of every case of consumption in the State without inflicting any hardship whatever upon any individual, inasmuch as the records are absolutely secret,

and no one outside of the board can possibly learn the names or localities of those reported. But it gives to the board a control over the situation which it can use to the welfare of the whole community. Coupled with this law and supplementing it is another of equal importance, making it possible for the boards of health to do the best kind of preventive and relief work in cases where the attending physician does not care to undertake the task.

This law directs the local boards of health to furnish antiseptics, paper napkins, spit cups, and necessary information to all consumptives unless the physician in attendance supplies these articles. It is hard to see how wiser provisions could have been made, and the good which results to many poor families, ignorant and unable to provide for themselves, is immeasurable. No State in the Union has a better law than this to enable the authorities to control and diminish tuberculosis.

Moreover, we have, too, a State laboratory established by law where the sputum from any patient in the State may be examined free, for the presence or absence of the germs of tuberculosis. This law enables the poorest patient in the State to have the advantage of the latest laboratory methods in the diagnosis of his case. No better opportunities through private laboratories can be given to the very richest. And still another law of which we boast is that forbidding spitting either on the sidewalks or in public conveyances or public places. When we recall that dried sputum is probably one of the principal sources of danger in transmitting tuberculosis from one person to another, the importance of this law cannot be overestimated.

Following these wise provisions, the last legislature took the next logical step in the crusade; namely, to appropriate money for the erection of a State sanatorium.

It is the hope of the board of managers of this sanatorium for *early* cases, those in which the chances of complete recovery are excellent, that it will be ready to receive patients by December of this year. A beautiful tract of land has been secured in the Blue Ridge Mountains at an altitude of 1500 feet, and already the plans for the buildings are well advanced. In the beginning its capacity will be small, and the utmost care must be exercised in selecting suitable cases for treatment, for it can well be seen that if but 64 beds are at first available, the utmost caution must be exercised to fill them with the patients likely to receive the greatest amount of good. It is a sad fact, and one needing especial emphasis, that of the patients applying for admittance to the sanatoria already in existence, scarcely more than one-third are in the early or incipient stage from which there is any great likelihood of recovery; it strikes one, therefore, with redoubled force, that somewhere grave mistakes are being made. When *our* State sanatorium is in operation I hope it will not have to report, as those of New York and Massachusetts have just reported, that only 40 per cent of its beds are occupied by the kind of patients for whom these institutions were built.

May I not appeal to the medical profession of Maryland to consider the gravity of delay in making a diagnosis of tuberculosis—and may I not appeal to all who find themselves run down with cough, fever, or malaise, that they hasten to learn the true nature of their disease; not to content themselves with having it called "a touch of bronchitis" or some other trifling malady, but rather to make sure, as did a patient at the Mt. Airy Camp, who, feeling that his physician had erred, himself sent his own sputum to the State laboratory only to learn in truth that he had tuberculosis. Fortunate for him, his distrust and his energy, for after six months open-air life at the Mt. Airy Camp, he was able to return home, and now, nearly two years later, is perfectly well and at work. If the life of a young, active man is estimated to be worth $2500, as is determined by the insurance companies, then the life of this one patient more than paid for all the expenditures of construction at Mt. Airy, an expenditure which was so generously made by the Quarter Club of Young Ladies of Baltimore.

In most of the large, and in many of the smaller, communities of the world, associations or their counterparts have been formed for conducting a campaign of education as to the nature of tuberculosis, how it can be prevented and how it can be cured. In this particular also Maryland has undertaken her responsibility. Inaugurated by the Tuberculosis Commission, of which Professor Wm. S. Thayer has been the efficient head, we have a very strong and active association with headquarters in Baltimore and with auxiliary associations in at least three counties of the State. The membership of the association is wholly unrestricted and should include every public-spirited man and woman of the State. For three years this association, by means of literature, lectures, reports, meetings, etc., has been spreading the knowledge of the infectiousness of tuberculosis and how it may be avoided; moreover, it has interested itself in observing the execution of the State and municipal laws and has proved of assistance to the Board of Health in moulding public opinion to an acceptance of these laws, particularly that most beneficial one, the disinfection of all houses after the death or removal of a case of "open" tuberculosis. While there is in some quarters a feeling that this law is prone to excite a false sense of security, there can be no doubt of its value if faithfully executed. The germs of consumption lurking in the dark corners of rooms occupied by consumptives are so likely to transmit the disease to the next occupant that tuberculosis is often spoken of as a house disease—one member after another of the same family becoming infected in this way and new occupants having the disease handed on to them unless the most thorough disinfection is practised.

In all this work we are fortunate in having State and city boards of health interested and energetic in carrying out to the fullest their part in the fight. The city board is paying especial attention to fumigation, while the State board is ever mindful of the problem in its widest aspects. Perhaps to no single person does the community owe so much as to the secretary of the State Board of Health. He has been the one to suggest many beneficent laws and he has been most instrumental in their enforcement. His, too, was the idea of the

tuberculosis and milk exhibits, which did so much to show our people the prevalence of consumption and the inferior, if not dangerous, quality of our milk.

The allied associations, that for the Improvement of the Condition of the Poor and the Charity Organization Society, are powerful factors, too, in our midst in this warfare which is being waged. The amount of relief the former has given in the nature of a diet of milk and eggs to many a poor patient is only known to the agents of the society. The reports show that in the past few years thousands of dollars have been expended in this deserving way.

For the past year two trained nurses in addition to the one supported in connection with the Phipps Dispensary, have been giving their entire time to the poor consumptive patients in the city. One has been supported by funds raised by Mrs. William Osler, the other by contributions of the Nurses' Association of Maryland. No factor in the city is more instrumental for the good of our cause than these nurses. They not only aid the sufferers, but they assist and encourage the members of afflicted families and others to seek advice and avoid the disease. In this way many an early case has been brought to the attention of the dispensary physicians, and so at a time when they had a chance for cure they have been sent to the sanatorium. It is from this class of patients that we are now at Eudowood getting our first truly hopeful incipient cases.

But in the great fight against the evil in our midst, I conceive our greatest asset to be the enlightened and interested public opinion which exists nowhere to a greater extent than right here in our own resurrected Baltimore. We do not need to be told, as were the people of Great Brtain when the Prince of Wales returned from his Indian tour, "Wake up." We are already awake, and, moreover, we have ourselves clothed and armed, determined to make effective our ideas and our hopes, watchful that our police department enforces to the letter the ordinance against spitting, that our board of health disinfects and fumigates beyond a shadow of criticism every infected home, and that our physicians evade not the law in reporting all cases of "open" tuberculosis coming to their attention. A striking illustration of the awakening of the community is found in the recent magnificent gift of Mr. Epstein to the Associated Jewish Charities for a consumptive hospital and in the eagerness with which his colleagues are subscribing $500 annually for its support.

The value of the campaign just finished has been greater than the $10,000 collected, and were it to be buried out of sight forever, our community would have received the full worth of its money in the awakened interest it takes in combating this plague; but instead of being buried it is going to be put into the most effective channels for carrying out the purposes of its collection—channels in which not only will the fence of prevention be fostered and strengthened, but also the more philanthropic and humanitarian sides of the work be developed. We expect to put into the field three new nurses whose work shall be exclusively among the poor of the city afflicted with tuberculosis.

We mean to encourage the establishment in the more remote and thickly settled portions of the city, such as Southeast Baltimore, of dispensaries, which will serve such neighborhoods as do the Phipps and University of Maryland dispensaries in the quarters where they are situated. Moreover, we hope to form a permanent exhibit illustrating tuberculosis in all its phases, pathological and economical—its means of prevention and cure. This exhibit, with a competent person to illustrate its features, will be displayed in various parts of the State, visiting at least every county seat. By such a method as this, we are confident a much wider appreciation of the ravages of tuberculosis will be gained. The distribution of literature and the giving of talks in all parts of the city and State will continue, and a closer alliance with workingmen's leagues, mutual benefit societies, and trade-unions, and other such organizations, will be encouraged.

In general, this is the situation in Maryland to-day, but what then is the next step? It is this, we must provide for advanced cases. Massachusetts has recently had a commission to study the problem, and it has recommended that three hospitals for advanced cases be built in various parts of the State—each of a capacity of 150 beds. Here in Maryland no side of our work needs such important development. The tuberculosis nurses feel especially this necessity, for they are constantly meeting with poor sufferers too advanced to be sent to the sanatoria, and too poor to be able to provide for themselves necessary comforts at home; moreover, these patients are the greatest menace to their family and the community, many of them being too ignorant to appreciate their danger to others, many more too ill to care. By the action of the last legislature the State has shown it appreciates its responsibility in the tuberculosis movement, and we shall look to the next legislature not only to carry on what is now so well begun, but to take this next step forward for the welfare of the whole people. In a measure each separate community should make provision for its own advanced patients, who are often too ill to be taken far from home, but need rather to be cared for in some nearby spot easily accessible to friends and relatives.

Hospitals receiving State aid may well determine to set aside a number of beds for such cases as these. Private charity cannot undertake this work to any great extent, but private philanthropy should be appealed to to the extent of its ability. We have in contemplation at Eudowood a hospital for 40 or 50 advanced cases, but this will do but little toward accommodating the many patients of this class in Baltimore alone, whereas if the State and the State-aided hospitals will give attention to this important side of the work, the conditions can soon be materially improved.

The low mortality from consumption in London is ascribed by many to the fact that for many years that city has been caring for its advanced cases. No state and no community can any longer consider that they have done their full duty in this crusade until they have provided amply for these distressing cases which furnish the great supply of infectious material for the continuance of the plague.

And what is the second step? It is to limit the supply of this infectious material which comes to us daily in our milk.

We must have more thorough State or municipal inspection of this product. Gradually the idea is spreading, whether it be wholly true or not, that the number of people, especially children, who take the disease from milk from tuberculous cows is large. There are opponents to this theory, but we cannot afford to run risks. Examination shows that the dairy cows of all states are very seriously infected and the milk of such cows, whether the udder itself be diseased or not, may contain tubercle bacilli. In one dairy herd in Rhode Island tested with tuberculin by The Newport Association for the Prevention of Tuberculosis 27 out of 39 cows, I think I have the figures right, showed themselves tuberculous, and every cow proved at autopsy that the test had told the truth. Is it not probable that we here in Maryland are using milk from herds of cows as seriously diseased? The thought alone is most repulsive, but the danger is most grave. Individuals cannot differentiate the contaminated from the pure milk, and so it is the urgent duty of both city and State to take the necessary precautions to protect their people. A law should be passed at the next legislature that no milk coming from dairies where all the cows have not been proven free of tuberculosis by the tuberculin test shall be publicly or privately sold. This would mean the slaughter of many cows, and in the loss to the farmer and dairy-man the State should be willing to bear a part of the expense for the sake of the safety of its citizens. With a pure milk supply and the meat of animals so carefully inspected that tuberculous flesh is not sold, a great advance will have been made.

Until within a few years the disease was not, in the minds either of the doctors or of the laity, commonly associated with children. We thought of them as having other forms of tuberculosis, especially the so-called surgical tuberculosis of bones, glands, etc., but not of the lungs. How children not living in immediate association with tuberculous families or individuals catch tuberculosis has been, and is, a subject of much careful study; if from cow's milk, then better there were no milk if it cannot be pure; but it can be pure and clean; it is only a question of healthy cows and clean handling, and both ends are easily attainable. Miss La Motte, one of the district tuberculosis nurses of this city, reports 29 children with consumption in her district. Children in the early stages of tuberculosis are prone to recovery, but what are we doing here in Maryland for these children? A few private associations are giving summer outings to a limited number, that is all. France, which leads the world in this respect, as in so many others, already has between 6000 and 7000 sanatorium beds for children with tuberculosis,—sanatoria at the seashore, especially for the surgical cases, and sanatoria in the country for consumptives.

But there is another side of the problem which claims attention. We may diminish the number of germs, we may care for the hopelessly ill, we may cure the early afflicted, but we must also take such care of the *well* that they may resist the attacks of the hidden foe. This can be done only by insisting upon the employment of all the factors which contribute to a perfectly sound body. Sanitation in all its forms: maximum of sunshine and air in all our dwellings, workshops, and schools; wider, better-paved, and cleaner streets; more parks and playgrounds; pure water supply and good drainage; better housing conditions; more food and that better cooked. All such factors as summer homes for children, playground associations, garden cities, and many other associations occupied with bettering conditions, are aiding the work, but it seems to me we must look to the schools for our progress in the near future. The boys and girls of to-day are the men and women of a few years hence. If as children they learn the lesson thoroughly they will be able to practise it when grown. I believe no question is so important as to teach the children how to avoid tuberculosis—is there anything more weighty for them to know? Do not reading, writing, and arithmetic sink into insignificance in comparison with the knowledge of how to live so as to live? What may be the best method for teaching this knowledge I am not prepared to say; the text-books upon physiology now in our schools are excellent, but they do not go far enough, they do not lay sufficient stress on the problem of how to live healthy. There must be a personal note put into this teaching, one that will strike home into every child's thoughts, one that will find such a lodgment there that habits of health will become automatic, as are so many other facts of education learned in childhood. Some form of objective teaching might be introduced successfully; for example, permanent tuberculosis exhibits simple in character, illustrating the value of cleanliness, exercise, and open air; this surely would be worth trying. Our schoolhouses should be, more than they are, centers of knowledge where parents as well as pupils could be taught the many lessons they should know. There is still one other class of school children and young people who should be more carefully looked after than they are. In France again they are ahead of us in this matter. I refer to those who may be styled the pre-tuberculous, *i. e.*, those who from one cause or another have become so run down, pale, weak, and debilitated that they are likely to become tuberculous. If taken in time these can be saved—a few months in the open air will do it. In Germany and in France they have established schools in the country or parks for the pupils of this class. In this way every year a large number are prevented from getting tuberculosis by increasing at a critical moment the powers of resistance. This is something we might do here.

But there seems no end to what we can and ought to do. Day camps for those who cannot leave home at night—night camps for sleeping out-of-doors for those who must work in the day-time and have no means of sleeping out at night—much more interest on the part of employers of labor in their employees—letters like the following, which was written by a large manufacturing shoe house to all its hands:

Oxford, Mass., March 1, 1906.

During the year 1905 no death from consumption is known to have occurred among the employees and their families of the factory. It is hoped that this good record will continue. To that end your attention is called to the following facts concerning consumption, and in particular to the occurrence of consumption in Oxford.

Consumption is a contagious disease. It is transmitted almost entirely by the sputum which is coughed up. This dries, and the dried particles containing the germs then float about in the air or are deposited upon neighboring objects. If these get into the body, consumption may result. The destruction of the sputum prevents the spread of the disease, and does it so surely that in consumptive hospitals nurses almost never take it.

Consumption has caused more than one death out of six in Oxford during the last sixty years. In the last thirty-five years it has greatly decreased, and at present only one-third as many people die of it as thirty-five years ago. In the last five years the decrease was as great as in the preceding ten years, and there is a good prospect that it can be stamped out, if all realize how it spreads. There were but four deaths from consumption in Oxford in 1905.

There are about 600 houses in Oxford, and in over one-third of this number some one had died of consumption. As a rule, one death has been followed by another. This would not have taken place if all the sputum had been burned. If the rooms in which a person with consumption has lived are thoroughly cleaned and aired, and opened to the sunlight, there is little danger that anyone will then get the disease from living in them.

Consumption spreads in families only because the members live together, and so infect one another. Living together is more important than relationship. In the sixty years, 1844-1904, 512 deaths from consumption in Oxford occurred in as many as 403 different families. One of these was as follows: A mother and three daughters died of consumption within three years of each other, in the same house; the father then moved away, but fell a victim to the disease a year later. Compare the above family with this typical instance of "farm-house consumption" in Oxford: A young man of twenty-one died in 1879 on a farm; seven years later his sister died in the same house; their mother died after another interval of eight years, also in the same house; and a year later another of her sons; three years later still another brother similarly succumbed, but in a different dwelling.

Consumption can be avoided. To do this, help all who have the disease to keep their houses clean, and show them how to destroy their sputum; then they will not give you the disease. Encourage everyone to open his windows, let in the sunlight, and stay out of doors whenever he can.

If you have a cough, see the doctor, and have your sputum examined for germs of the disease. One examination is not enough. The State Board of Health will examine sputum for nothing.

The firm hopes that it will be notified of any case of consumption occurring among the employees or their families. If anyone now in the employ of the A. L. Joslin Company has the disease, or contracts it, and secures the admission this year to the State Sanatorium at Rutland, the firm will offer to pay his or her board there for three months.

A. L. Joslin Company.

Nor can we neglect the colored population of the State either upon philanthropic or on economical grounds. They are particularly susceptible to infection, and their habits and manner of life make them a source of danger in the community. They are working in almost every house and whatever is for their welfare is for the welfare of all. We need institutions where the early cases may be treated, but more especially we need hospitals where the more advanced cases may be segregated. We cannot hope to stamp out tuberculosis from Maryland until we have provided for the colored race as well as the white. It may take some years, but just as smallpox was overcome in the early years of the last century, so I believe it possible that tuberculosis may be in this. God grant this may not be a futile hope.

INTESTINAL OBSTRUCTION.[1]

By Joseph C. Bloodgood, M. D.

Stimulated, probably, by some interesting recent cases, I felt that a careful clinical and pathological investigation of the experience of Dr. Halsted's clinic of the Johns Hopkins Hospital, of intestinal obstruction, would at least be valuable to myself. It proved to be of such interest that I presented some of the conclusions before the New York State Medical Society, in Albany, January 30, and do not hesitate to repeat them again to-night.

The conclusions in regard to the importance of early intervention in all cases and the life-saving measure of enterostomy in late cases, I find is confirmed by Rubritius (Beiträge zur klin. Chir., 1906, vol. lii, p. 405) from Wölfler's clinic in Prague, by Simon (Beiträge zur klin. Chir., 1905, vol. xlv, p. 489) from Czerny's clinic in Heidelberg, and by Göbell (Deutsche Zeitschr. f. Chir., 1906, vol. lxxxii, p. 416) from Helferich's clinic in Kiel.

"Intestinal obstruction" should be employed as a general term and corresponds to the German term "ileus." All authorities recognize two groups—*strangulation ileus,* in which, in addition to obstruction to the lumen of the intestine, there is interference with the mesenteric blood supply; and *obturation ileus,* in which the blood supply of the obstructed portion of the intestine is not disturbed. In some cases the intestinal obstruction may begin as an obturation and end as a strangulation.

It is quite true that in obturation ileus the patients may survive a longer period from the onset of the symptoms to the time of operative relief. Nevertheless, in either group immediate surgical relief gives the best results.

The older view favoring delay in obturation ileus is emphatically discredited by all recent contributions. Intestinal obstruction from its onset should be looked upon as a surgical lesion, and no conservative means should be employed for its relief, except the washing out of the stomach and high rectal enemata. These should be used only in the early hours; and if relief is not immediate, the abdomen should be opened. Any food, liquid or solid, or cathartics by mouth, is absolutely contra-indicated, from the moment of the first symptom until the patient is relieved. Morphia should not be given for the pain unless operation has been decided upon.

[1] Paper read before the Medical and Chirurgical Faculty of Baltimore.

These rules, simple as they may appear, have seldom, if ever, been followed with patients admitted to surgical wards. In the three contributions from the German clinics just mentioned, and in many other articles on special forms of ileus, the writers call attention to the delay after which these patients are referred to the surgeon, to their previous drastic treatment with cathartics, and to the masking of the symptoms with large doses of opium.

I found the same to be true in a series of cases admitted to the surgical clinic of the Johns Hopkins Hospital.

Intestinal obstruction is a relatively infrequent disease. Among about 20,000 patients admitted to the surgical clinic I find but 103 instances of ileus, and rarely have two of these cases come from the practice of the same physician.

The general practitioner, therefore, will be called upon to attend this lesion only at rare intervals. It should be the duty of surgical clinics, whose collective experience is so much larger, to instruct the physician on the symptoms of onset, and to demonstrate to him by irrefutable figures that their patients' chances are tremendously increased by operative interference, if possible within the first 24 hours, at least before the end of the second day. The more acute the symptoms of onset the more immediate must be relief. It is fortunate that in strangulation ileus, in which the earliest intervention is required, the symptoms of onset are most acute and characteristic, while in oburation ileus the clinical picture is most obscure, requiring sometimes a few days to make the diagnosis. Fortunately, if the delay of relief is not too long, the chances of recovery are good.

Surgeons are in a better position than physicians to study the early clinical picture of intestinal obstruction. After every laparotomy this complication must be borne in mind. All post-operative patients receive unusually critical investigation, if any symptoms suggestive of obstruction arise. That surgeons have become more expert in the diagnosis is borne out by the fact that in Dr. Halsted's clinic, and in observations of my own in other hospitals, post-operative intestinal obstruction has been recognized early, and the mortality is strikingly less than in the group of patients first observed outside the clinic and then referred for operative treatment. It is due, then, to this fact that one feels justified in speaking so emphatically to the general practitioner.

In strangulation ileus there are two factors which give rise to symptoms—obstruction to the flow of intestinal contents, and interference with the circulation of the obstructed intestine. It is the interference with the blood supply that gives the acute symptoms of onset in strangulation ileus: the intense pain, the peritoneal shock, and the primary reflex vomiting. Secondary vomiting, fecal in character, and distention are symptoms due to the obstruction and may be looked upon as late symptoms—symptoms which one should not wait for in order to make a diagnosis. In obturation ileus the symptoms of onset present in strangulation are usually absent. The patient may complain of some abdominal pain, which is described more as a general discomfort than as acute agony. It is constipation that first attracts his attention, then distention, then vomiting, which may, in delayed cases, be fecal in character.

It is frequently difficult to explain the exact cause of pain and its acuteness in a strangulation ileus. We know that the intestine is insensitive. One interested in the sensitiveness of the peritoneum and abdominal viscera and the explanation of intestinal colic, should read Lennander's (Mittheilungen aus d. Grenzgeb. d. Chir. u. Med., 1906, vol. xvi, pp. 19 and 24) and Wilms' (Ibid., 1906, vol. xvi, p. 609) recent communications. There is no question as to the pain in strangulation ileus, and apparently it is not due, in its onset, to increased peristalsis. It is probably explained by the pull on the mesentery or the interference with its blood supply which affect the sensitive nerves at the mesenteric base. For example, I have seen a number of instances of strangulated inguinal or femoral herniæ of the Ritter variety. Here the wall only of the gut is caught. These patients complain very much less of pain than those in whom the mesentery participates in the strangulation. The pain in strangulation ileus is not always localized in the position of the strangulated gut, but is referred to some other part of the abdomen. In two recent cases of acute volvulus of the sigmoid colon under my own observation, the pain was referred to the region of the left kidney, which corresponds to the origin of the nerves supplying the mesosigmoid. When peristalsis takes place, either in strangulation or in obturation ileus, the pain becomes intermittent or colicky in character. The cause of this pain of intestinal colic has not been satisfactorily explained. The most characteristic symptom, then, of strangulation ileus is the sudden, intense abdominal pain. If situated in the right iliac fossa it may suggest appendicitis; in the gall-bladder area—gall-stone colic; if in the region of the kidney—renal colic. In my two cases of acute volvulus of the sigmoid the pain alone could not have been differentiated from that due to a stone in the kidney; in one it was referred to the testicle. A patient, therefore, who complains of sudden abdominal pain of such intensity that he begs for relief should be examined most critically, and the possibility of an acute lesion demanding early operative relief should be considered. In the pain from strangulation ileus the shock is more marked than that observed in those cases associated with appendicitis, gall-stones, or renal calculus. As a rule the shock is not so severe as that seen in acute hemorrhagic pancreatitis.

In the two cases of acute volvulus above referred to the immediate and quite distinct shock following the pain was of great value in excluding renal calculus. The primary nausea and vomiting are undoubtedly reflex in character. These symptoms are not at all characteristic of obstruction, and may be present in any acute abdominal lesion.

If the patient complaining of severe abdominal pain, nausea, and vomiting, is examined, one will find some symptoms of shock—the pulse is rapid, the face is pale, and the patient will state that he feels distinctly weak, as if he has been kicked in the abdomen, while the moment before the attack of pain he may have been in the best of health and strength. If the abdomen is now carefully examined, one does not find the localized

tenderness and muscle spasm, early signs in appendicitis and cholecystitis, but a more general muscle rigidity without tenderness; now and then the distended loop above the strangulation can be palpated (von Wahl's sign). If this is situated in the pelvis it is felt per vaginam or rectum. The palpation of the distended loop may be looked upon as the pathognomonic symptom of strangulation ileus, but it can be distinguished only in the early hours before general distention obliterates it. In the recent case of acute volvulus of the sigmoid seen six hours after the onset the only symptoms were: pain in the region of the kidney, nausea, and slight shock, which had been more marked in the first two hours. Although all the abdominal muscles were held rigid, the patient complained absolutely of no tenderness. The muscles on the left side were more rigid than those on the right. Yet there was absolutely no tenderness over the sigmoid. After a very careful palpation, I could make out, I thought, a distended loop.

The next sign in strangulation ileus to which Schlange first called attention in 1895 is peristalsis. There is no doubt as to the interpretation of this symptom if it can be demonstrated.

How often peristalsis can be made out in strangulation ileus is impossible to state. It has been present and recorded in a certain number of cases early in the attack. The older view that peristalsis did not take place when the gut was strangulated has therefore been refuted. I have observed it early in post-operative obstruction, when the small intestine was involved, I have seen it in intussusception of the ileo-cecal type, and it was present in a few cases of strangulation by bands which I had the good fortune to observe within the first 24 hours. It is always absent in the late cases of the strangulation type, that is, when the small intestines are distended and to a certain degree paralyzed. One, therefore, should not wait for peristalsis, nor consider its absence as excluding obstruction.

In my own experience which I have referred to in 1901 (Transactions of the American Surgical Association, vol. xix, p. 139) a leucocytosis is a very important aid in the early recognition of intestinal strangulation. I think my colleague, Dr. Harvey Cushing, was the first to call attention to this fact in Dr. Halsted's clinic in 1898. I mentioned this in a report on hernia (Johns Hopkins Hospital Reports, vol. vii, p. 332). Since then all the surgeons connected with this clinic have made blood-counts in cases of suspected strangulation, primary or post-operative, and have confirmed the early experience. The cases of acute volvulus which I have mentioned here a number of times had a leucocyte count of 34,000 three hours after the onset. I have to thank Dr. Shaw of St. Agnes Hospital for this early observation.

Complete constipation is always present, but if the patient has not had a stool for a day or two before the onset of the acute attack, the first enema may bring away fecal contents; but this gives no relief, and after this repeated enemata are ineffectual.

In strangulation ileus, to summarize, the patient complains of acute abdominal pain, sudden in onset, with no previous premonitory symptoms—the first attack, as a rule. Reflex nausea and vomiting, and peritoneal shock rapidly follow. If it is some hours after a meal the vomitus contains nothing but the normal contents of the stomach, or if shortly after a meal, partially digested food. Now and then the sudden pain comes so quickly after a large meal or indiscretions in diet or liquid that the patient attributes his pain to this fact. The pain continues, and if the patient is seen early, one will find symptoms of shock. An enema, whether effectual or not, gives no relief. If the patient has vomited a stomach washing is negative. The abdominal muscles are held somewhat rigid, and the rigidity is most marked in the region of pain. There is no abdominal tenderness. Examined carefully, von Wahl's loop or peristalsis may be made out. The blood-count will show a leucocytosis. If one or all of the three latter symptoms are present the diagnosis can be made. If the three latter symptoms are absent such a patient should receive nothing by mouth, the only treatment should consist of high enemata. If these are ineffectual and the symptoms persist surgical consultation is indicated. I believe a careful examination in the early hours will demonstrate the characteristic signs—the palpable loop, the peristalsis, or the leucocytosis. This, with the initial symptoms and the continuing absence of feces or gas per anum, is sufficient to indicate immediate operation. In post-operative cases surgeons do not delay, but at the present time unfortunately few patients are admitted to the surgical clinic in this early stage. The later symptoms are: fecal vomiting, general abdominal distention, continuing absolute constipation, and the signs of autointoxication. Now the diagnosis is simple, but the chances of recovery, even though the operation be performed early in this stage, are few.

In obturation ileus the acute primary symptoms are frequently absent. There is often a previous history of constipation and abdominal colic. In carcinoma of the large intestine there may be a history of blood in the stool, or intermittent diarrhœa and constipation. In this group of obturation ileus, I have been impressed with the history of recurrent attacks of intestinal obstruction,—that is, absolute constipation, vomiting (not fecal), and distention,—which have been relieved after a day or two by cathartics and enemata. This history of a successful non-operative relief often puts the physician off his guard and operative interference is delayed. In one of my own cases there was a history of five such attacks, one lasting five days. In obturation from carcinoma of the large intestine the obstruction of the lumen may not be absolutely complete, and some little fecal matter and gas may pass, appear in the enema, and if this symptom is interpreted as a sign of relief the necessary operation is often further delayed. When the obturation is in the small intestine, peristalsis is a constant early symptom. If the obstruction is high in the small intestine distention is slight or absent and vomiting of a fecal character early. In obturation the symptoms are more obscure than in strangulation ileus, but the constipation, even though there be no vomiting or peristalsis, should be regarded as suspicious; the following distention, even without vomiting, as still more suspicious. In obturation of the colon the

distention may be extreme before vomiting takes place. This clinical picture with the evidence of some gas and feces in the enema should be enough to allow a diagnosis of an obstruction of the large intestine. Early vomiting and absolute constipation, sometimes without much pain and with little or no distention, indicate an obturation of the small intestine high up; peristalsis can usually be made out.

I have not mentioned movable dullness in the abdomen. It is practically absent in obturation ileus, and is a late sign in strangulated ileus.

From my own experience in post-operative obstruction, and from the few cases that I have seen in the early hours of primary intestinal obstruction, I believe that it is not difficult to make a diagnosis at a period in which operative intervention promises an excellent chance of recovery. If the practitioners will avoid giving cathartics indiscriminately, place such patients in bed, give them nothing by mouth, employ the stomach tube and rectal enemata early, make a careful abdominal examination and blood-count, and avoid morphia if possible, I feel quite confident that they will be able to recognize intestinal obstruction in the early hours. If the intense agony demands some relief before a decision as to operative intervention can be made, small doses of morphia may be given. This has been accomplished in appendicitis, and in perforated gastric and duodenal ulcer; why not in intestinal obstruction?

The problems in the surgery of intestinal obstruction present increasing difficulties with the duration of the attack and the possible complications. In strangulation ileus peritonitis may take place without gangrene or perforation; autointoxication must be considered in all late cases.

Before operation the stomach should be washed out. Chloroform may be the best anesthetic. The anesthesia must be very carefully induced. The washing out of the stomach does not always prevent vomiting under narcosis, and in such cases chloroform is better than ether. The selection of the position of the incision varies. If the exact position of the obstruction cannot be fixed, median laparotomy should be performed. In desperate cases a simple enterostomy under cocaine may have to be done. This is only feasible in obstruction of the large intestine, or low down in the ileum. If possible, the obstruction should be found and relieved. If the intestine above the point of obstruction is distended and filled with fluid contents, it should be evacuated; and if the symptoms have been present over 48 hours, enterostomy should be performed in addition to the relief of the obstruction. The mortality of operation after 48 hours without enterostomy is so definitely higher than with enterstomy, that there appears at this time no question as to the efficacy of this additional safeguard. The object of the enterostomy is to aid the patient in immediately disposing of intestinal contents and combating autointoxication. When the intestine is the seat of gangrene, the gangrenous loop must be taken out of the abdominal cavity. The surgeon has to decide between fixing the loop outside of the wound with enterostomy above, and later resection, or resection at once with fixation of the ends in the wound, and resection with suture. This decision is reached in individual cases. When there is obturation from a new growth, one must decide between enterostomy or colostomy alone with a later operation for resection, and immediate resection. The earlier the operation takes place after the initial symptoms the easier to settle these questions, and the more frequently can the lesion of the intestine be relieved completely at one operation with the least mortality.

THE PURPLE ISLAND BY PHENIAS FLETCHER.

A SEVENTEENTH CENTURY LAYMAN'S POETICAL CONCEPTION OF THE HUMAN BODY.

By Augustus Grote Pohlman, M. D.

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The Purple Island by Phenias Fletcher (1582-1650) was first published in 1633; again in 1784; a third time in 1816, and the last edition (at hand and limited to 106 copies) in 1869. While authorities seem to believe that Fletcher's poetry influenced that of the immortal Milton, they appear to regard his work as stilted. The Purple Island, according to S. L. Lee, in the Dictionary of National Biography, is an allegory "overloaded with detail, and as a whole is clumsy and intricate." Nevertheless the poem is to be looked upon with interest in that the first five cantos contain a dissertation on the human body in verse, and in that they furnish us with an idea of how well a layman understood the structure of self at that time. The Purple Island is not an accessible book, and for that reason I offer some of the better verses, illustrating particularly apt descriptions, together with a meager account of the scope of the work.

"Thirsil" (Fletcher himself) sings of the wonders of the body to the "nymphs and shepherd-boyes." The creation is naturally Genesis:

> "Nor made He this like other Isles; but gave it
> Vigour, sence, reason, and a perfect motion,
> To move it self whither it self would have it,
> And know what falls within the verge of notion:
> No time might change it, but as ages went,
> So still return'd; still spending never spent;
> More rising in their fall, more rich in detriment."—I, 46.

> "Looke as a scholar, who doth closely gather
> Many large volumes in a narrow space;
> So that great Wisdome all this All together
> Confin'd into this Island's little space;
> And being one, soon into two he fram'd it;
> And now made two, to one again reclaim'd it;
> The little Isle of Man, or Purple Island nam'd it."—I, 48.

In Canto II the description of the body begins with bone, cartilage, and ligament.

"It grounded lies upon a sure foundation,
Compact, and hard; whose matter—cold and drie—
To marble turns in strongest congelation;
Fram'd of fat earth, which fires together tie:
Through all the Isle, and every part extent,
To give just form to every regiment;
Imparting to each part due strength and stablishment."
—II, 5.

"Whose looser ends are glu'd with brother earth,
Of nature like, and of a near relation;
Of self-same parents both, at self-same birth:
That oft it self stands for a good foundation:
Both these a third doth soulder fast, and binde;
Softer than both, yet of the self-same kinde;
All instruments of motion when combin'd."—II, 6.

He goes on to mention the muscle mass and coverings of the body, but takes these up in greater detail later. The first allusion to the circulatory system is as follows:

"Nor is there any part in all this land,
But is a little Isle: for thousand brooks
In azure chanels glide on silver sand;
Their serpent windings and deceiving crooks
Circling about, and wat'ring all the plain,
Emptie themselves into th' all-drinking main;
And creeping forward slide, but never turn again."—II, 9.

It might be inferred that Fletcher knew of Harvey's work published five years before the printing of the Purple Island. Further reading shows that this is not the case, and also is substantiated in the prelude: "I am entring upon my Winter, and yet these blooms of my first Spring." It is thought that Fletcher started the work while at Cambidge where he entered in 1600.

The Island is parted in three regiments, "By three Metropolies joyntly sway'd," namely, the abdomen, chest, and head—with liver, heart, and brain as "chief cities," respectively. He describes the five layers of the abdominal wall:

"The first of these is that round spreading fence,
Which like a sea girts th' Isle in every part;
Of fairest building, quick and nimble sence,
Of common matter fram'd with speciall art;
Of middle temper, outwardest of all,
To warn of every chance that may befall:
The same a fence and spie; a watchman, and a wall."
—II, 16.

"It cover'd stands with silken flourishing,
Which as it oft decaies, renews again,
The other's sense and beautie perfecting;
Which els would feel, but with unusuall pain:
Whose pleasing sweetnesse and resplendent shine,
Softning the wanton touch, and wandring ey'n,
Doth oft the Prince himself with witch'ries undermine."
—II, 18.

It was not until Malpighi's time (1665) that the microscope made matters a little clearer.

"The second rampier of a softer matter,
Cast up by th' purple rivers' overflowing:
Whose airy wave, and swelling waters, fatter
For want of heat congeal'd, and thicker growing,
The wandering heat—which quiet ne're subsisteth—
Sends back again to what confine it listeth;
And outward enemies by yeelding most resisteth."—II, 19.

Even Malpighi seems to have been influenced by the popular notion as to the origin of fat when he saw minute globules floating in the blood stream and apparently leading from one fat mass in the omentum to another.

"The third more inward, firmer than the best,
May seem at first but thinly built, and slight;
But yet of more defence than all the rest;
Of thick and stubborn substance, strongly dight.
These three—three common sences—round impile
This regiment, and all the other Isle;
And saving inward friends, their outward foes beguile."
—II, 20.

"Beside these three, two more appropriate guards
With constant watch compasse this government:
The first eight companies in severall wards,
—To each his station in this regiment—
On each side foure, continuall watch observe,
And under one great Captain joyntly serve;
Two fore-right stand, two crosse, and foure obliquely swerve."—II, 21.

The verse on the peritoneum is accompanied by an interesting footnote which reads: "It hath many holes, that veins, arteries, and other needfull vessels might have passage both in and out." If by "other needfull vessels" Fletcher meant the lacteals discovered by Aselli in 1622, but not published until 1627 does not appear. It is probable that he meant the nerves.

"Between this sence's double-walled sides,
Four slender brooks run creeping o're the lea;
The first is call'd the Nurse, and rising slides
From this low region's Metropolie:
Two from the Heart-citie bend their silent pace;
The last from Urine-lake with waters base
In th' Allantoid sea empties his flowing race."—II, 23.

In his note on this verse he makes the following comment: "Where the vessels of the navile are contained. These are foure: first, the nurse; which is a vein nourishing the infant in the wombe; second, two arteries, in which the infant breathes; the fourth, the Ourachus, a pipe whereby (while the childe is in the wombe), the urine is carried into the Allantoid, or rather Amnion; which is a membrane receiving the sweat and urine." (Excellent knowledge for a clergyman.)

Six cities are found in this region: "The liver, stomack, with the guts; the gall, the spleene, or milt; the kidneys, and parts for generation.

Mastication and swallowing are mentioned. He believes in a definite sphincter—"the upper mouth of the stomack has little veins, or strings circular, to shut in the meat, and keep it from returning." The "Vas breve" is supposed to stir up "civile strife" and the spleen to be the seat of melancholy.

"The Island's common cook, Concoction" prepares the

food in the stomach by the aid of "moistning flames" sent it by neighboring organs. The "Porter" drains the kitchen, and he goes on to describe the intestines.

"These pipes are seven-fold longer than the Isle,
Yet all are folded in a little pile,
Whereof three noble are, and thinne; three thick and vile."
—II, 39.

"The first is narrow'st, and downright doth look,
Lest that his charge discharg'd might back retire;
And by the way takes in a bitter brook,
That when the chanel's stopt with stifeling mire,
Through th' idle pipe with pipe with piercing waters soking,
His tender sides with sharpest stream provoking,
Thrusts out the muddy parts, and rids the miry choking."
—II, 40.

"The foremost of the base half blinde appeares;
And where his broad way in an Isthmos ends,
There he examines all his passengers,
And those that ought not scape, he backward sends:
The second Æol's court, where tempests raging
Shut close within a cave the windes encaging;
With earthquakes shakes the Island, thunders sad presaging."—II, 42.[1]

The rectum and its sphincter are passed over hurriedly with the following words:

"This gate endow'd with many properties,
Yet for his office sight and naming flies;
Therefore between two hills in darkest valley lies."

The Epiploon, Mesenterium, and Pancreas are named. The function of the latter it will be remembered was not known at this time, and in fact it was regarded as more or less of a useless organ until Wirsung discovered the duct in 1643—some ten years after this book was published.

The description begins in Canto III with the Isle's great Steward—the liver: "To th' heart and to th' head-citie surely ti'd" as his note states to the heart by arteries, to the head by nerves (possibly the phrenics)—a connection between inflammation of the diaphragm and brain was mentioned by Galen, although stoutly denied by Alexander of Tralles, (see Puschmann's Alexander of Tralles, Vol. I, p. 510).

"Much like a mount, it easily ascendeth;
The upper part's all smooth as slipperie glasse:
But on the lower many a cragge dependeth;
Like to the hangings of some rockie masse:
Here first the purple fountain making vent,
By thousand rivers through the Isle dispent,
Gives every part fit growth and daily nourishment."—III, 7.

"Two purple streams here raise their boiling heads;
The first and least in th' hollow cavern breeding,
His waves on divers neighbor grounds dispreads:
The next fair river all the rest exceeding,
Topping the hill, breaks forth in fierce evasion,
And sheds abroad his Nile-like inundation;
So gives to all the Isle their food and vegetation."—III, 11.

"Yet these from other streams much different;
For others, as they longer, broader grow;
These as they runne in narrow banks impent,
Are then at least, when in the main they flow;
Much like a tree, which all his roots so guides,
That all the trunk in his full body hides;
Which straight his stemme to thousand branches subdivides."—III, 12.

"Yet lest these streams might hap to be infected
With other liquors in the well abounding;
Before their flowing chanels are detected,
Some lesser delfs, the fountain's bottome sounding,
Suck out the baser streams, the springs annoying,
An hundred pipes unto that end employing;
Thence run to fitter place, their noisome load convoying."
—III, 13.

He mentions the "controversie between the Peripateticks and the Physicians," and commits himself as follows:

"Such is fair Hepar, which with great dissension
Of all the rest pleads most antiquitie;
But yet th' Heart-citie with no less contention,
And justest challenge, claims prioritie:
But sure the Hepar was the elder bore;
For that small river, call'd the Nurse, of yore
Laid boths' foundation, yet Hepar built afore."—III, 14.

The three kinds of "excremental liquors"[2] were disposed of in verses 15, 16, and 17. It must of course be remembered that the work of Glisson and Malpighi did not appear until 1654 and 1661, and Malpighi had to contend with the idea that bile was formed in the gall bladder.

"Three pois'nous liquors from this purple well
Rise with the native streams, the first like fire,
All flaming hot, red, furious, and fell,
The spring of dire debate, and civile ire;
Which wer't not surely held with strong retention,
Would stirre domestick strife, and fierce contention,
And waste the weary Isle with never ceas'd dissension."

"Therefore close by a little conduit stands,
Choledochus, that drags this poison hence,
And safely locks it up in prison bands;
Thence gently drains it through a narrow fence;
A needfull fence attended with a guard,
That watches in the straits all closely barr'd,
Lest some might back escape and break the prison ward."

Fletcher comments on the last verse: "It hath two passages, one drawing the humour from the liver, another conveying the overplus to the first gut, and so emptying the gall. And this fence hath a double gate to keep the liquour from returning."

[1] "The first of the baser is called blinde: at whose end is an appendant, where if any of the thinner chyle do chance to escape, it is stopt, and by the veins of the midriffe suckt out."

[2] "The chyle, or juice of meats concocted in the stomack could not all be turned into sweet bloud by reason of the divers kinds of humours in it: Therefore there are three kinds of excrementall liquours suckt away by little vessels, and carried to their appointed places: one too light, and fiery; an other too earthy, and heavy; a third wheyish, and watery."

"The next ill stream the wholesome fount offending,
All dreary black and frightfull, hence convay'd
By divers drains unto the Splenion tending,
The Splenion o're against the Hepar laid,
Built long, and square: some say that Laughter here
Keeps residence, but Laughter sits not there,
Where darknesse ever dwells, and melancholy Fear."

"The third bad water, bubbling from this fountain,
Is wheyish cold, which with good liquours mient,
Is drawn into the double Nephros mountain;
Which suck the best for growth, and nourishment:
The worst, as through a little pap, distilling
To divers pipes, the pale cold humour swilling,
Runs down to th' Urine-lake, his banks thrice daily filling."

He foregoes a description of the genital organs under cloak of modesty:

"Forbear, my maiden song, to blazon wide
What th' Isle and Nature's self doth ever strive to hide."

Procreation, however, is aptly conveyed in verses 26 and 27.

"These two fair Isles distinct in their creation,
Yet one extracted from the other's side,
Are oft made one by Love's firm combination,
And from this unitie are multipli'd:
Strange may it seem; such their condition,
That they are more dispread by union;
And two are twenty made, by being made in one.

For from these two in Love's delight agreeing,
Another little Isle is soon proceeding;
At first of unlike frame and matter being;
In Venus' temple takes it form and breeding,
Till at full time the tedious prison flying,
It breaks all lets its ready way denying;
And shakes the trembling Isle with often painfull dying."

Canto IV deals with the middle province—the seat of "all heat and life" and "therefore walled about with ribs, for more safety."

"But in the front two fair twin-bulwarks rise,
In th' Arren built for strength, and ornament; [Arren the man]
In Thelu of more use, and larger size; [Thelu, the woman]
For hence the young Isle draws his nourishment:
Here lurking Cupid hides his bended bow;
Here milkie springs in sugred rivers flow;
Which first gave th' infant Isle to be, and then to grow."
—IV, 5.

"For when the lesser Island—still increasing
In Venus' temple—to some greatnesse swells,
Now larger rooms and bigger spaces seizing,
It stops the Hepar rivers; backward reels
The stream, and to these hills bears up his flight,
And in these founts—by some strange hidden might—
Dies his fair rosie waves into a lily white."—IV, 6.

A curious mistake, common even at the present time, is found in IV, 11.

"This third the merrie Diazome we call,
A border-citie these two coasts removing;
Which like a balk, with his crosse-builded wall,
Disparts the terms of anger, and of loving;
Keeps from th' Heart-citie fuming kitchen fires,
And to his neighbours gentle windes inspires;
Loose when he sucks in aire, contract when he expires."

The description of the heart is detailed. The Pericardium is mentioned as a "wheyish moat." The anatomy and physiology was derived for the most part from Galen and some from Vesalius, Columbus, and others. The coronary vessels are noted "two arteries, and a vein called the crowns." The heart is included in verses 18-24.

"The citie's self in two partitions reft,
That on the right, this on the other side:
The right—made tributarie to the left—
Brings in his pension at his certain tide,
A pension of liquours strangely wrought;
Which first by Hepar's streams are hither brought,
And here distill'd with art, beyond or words or thought.

The grosser waves of these life-streams—which here
With much, yet much lesse labour is prepar'd—
A doubtfull chanel down to Pneumon bear:
But to the left those labour'd extracts shar'd,
As through a wall, with hidden passage slide;
Where many secret gates—gates hardly spi'd—
With safe convoy give passage to the other side.

At each hand of the left two streets stand by,
Of severall stuffe, and severall working fram'd,
With hundred crooks, and deep-wrought cavitie:
Both like the ears in form, and so are nam'd.
I' th' right street the tribute liquour sitteth:
The left forc't aire into his concave getteth;
Which subtile wrought, and thinne, for future workmen fitteth.

The citie's left side,—by some hid direction—
Of this thinne aire, and of the right side's rent, [!]
—Compound together—makes a strange confection;
And in one vessel both together meynt, [mixed]
Stills them with equall never-quenched firing:
Then in small streams—through all the Island wiring—
Sends to every part, both heat and life inspiring.

In this Heart-citie foure main streams appeare,
One from the Hepar, where the tribute landeth,
Largely pours out his purple river here:
At whose wide mouth a band of Tritons standeth,
Three Tritons stand—who with their three-forkt mace
Drive on, and speed the river's flowing race,
But strongly stop the wave, if once it back repace.

The second is that doubtfull chanel, lending
Some of this tribute to the Pneumon nigh;
Whose springs by carefull guards are watcht, that sending
From thence the waters, all regresse denie:
The third unlike to this from Pneumon flowing,
And his due ayer-tribute here bestowing, [!]
Is kept by gates and barres, which stop all backward going.

The last full spring out of this left side rises,
Where three fair Nymphs, like Cynthia's self appearing,
Draw down the stream which all the Isle suffices;
But stop back-waies, some ill revoluture fearing.
This river still it self to lesse dividing,
At length with thousand little brooks runnes sliding,
His fellow course along with Hepar chanels guiding."

The function of the lungs was naturally restricted and not understood until the demonstration of the circulation by Harvey, even then imperfectly.

"Close by this pipe runnes that great chanel, down
Which from high Cephal's mount twice every day
Brings to Koilia due provision:
Straight at whose mouth a floud-gate stops the way,
Made like an ivie leaf, broad-angle-fashion;
Of matter hard, fitting his operation,
For swollowing soon to fall, and rise for inspiration."
—IV, 28.

The muscle tissue completing the tracheal rings dorsally had long been observed, but it was so arranged that "the meat pipe might not be galled or hurt."

"Fitly 'tis cloath'd with hangings thinne and light,
Lest too much weight might hinder motion:
His chiefest use to frame the voice aright;
—The voice which publishes each hidden motion—[? notion]
And for that end a long pipe down descends,
—Which here it self in many lesser spends—
Untill low at the foot of Cephal mount it ends."—IV, 32.

In verse 33 we meet another curiosity—"the unmoved gristle" of the larynx (cricoid?) often double in women.

"Upon the top there stands the pipes' safe covering,
Made for the voice's better modulation:
Above it fourteen carefull warders hovering,
Which shut and open it on all occasion:
The cover in foure parts, it self dividing,
Of substance hard, fit for the voice's guiding;
One still unmov'd—in Thelu double—oft residing."—IV, 32.

Canto V takes up the head-citie.

"Foure severall walls, beside the common guard,
For more defence the citie round embrace:"—V, 11.

"The other two of matter thinne and light;
And yet the first much harder than the other;
Both cherish all the Citie: therefore right
They call that th' hard, and this the tender mother.
The first with divers crooks and turnings wries
Cutting the town in foure quaternities;
But both joyn to resist invading enemies."—V, 12. [Brain membranes.]

Fletcher's knowledge of the brain, of the eye (the latter well described) as well as other parts of the head were undoubtedly drawn from the Greeks. The verse on the ear bones is particularly apt.

"The first an hammer is call'd, whose out-grown sides
Lie on the drumme; but with his swelling end
Fixt in the hollow stithe, there fast abides:
The stithe's short foot doth on the drumme depend,
His longer in the stirrup surely plac't;
The stirrup's sharp side by the stithe embrac't,
But his broad base ti'd to the little window fast."—V, 43.

The Labyrinth was well known, but apparently was supposed to contain air. Otherwise the mode of hearing was relatively well understood, as illustrated by the next two verses—taken, I believe, almost wholly from Galen, who, according to Puschmann gives a similar figure:

"As when a stone, troubling the quiet waters,
Prints in the angry stream a wrinkle round,
Which soon another and another scatters,
Till all the alke with circles now is crown'd:
All so the aire struck with some violence nigh,
Begets a world of circles in the skie;
All which infected move with sounding qualitie.
These at Auditus' palace soon arriving,
Enter the gate, and strike the warning drumme;
To these three instruments fit motion giving,
Which every voice discern: then that third room
Sharpens each sound, and quick conveys it thence;
Till by the flying poast 'tis hurri'd hence,
And in an instant brought unto the judging sense."
—V, 47 and 48.

These are the better verses of Phenias Fletcher's "Purple Island," and show a rather remarkable knowledge of the human body. It is hardly fair to say that Fletcher contributed anything to the art, except perhaps in his wording and his allusions. The description of the mode of hearing especially appeals to me as extremely simple and yet relatively well done. It must be remembered that apart from the Greek school, the only accessible works were possibly those of Sylvius, Vesalius, Fallopius, and Fabricius. That he must have known of the works of these men is to be inferred from the credited discovery of the stapes in 1548 by Ingrassias. It appears, however, quite extraordinary that the other ear ossicles—the labyrinth with its two windows—should have been known long before this time without the stapes being discovered.

The writer begs to acknowledge the kindness of Professor J. W. Bright, of Johns Hopkins University, in calling his attention to the "Purple Island."

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THE SIXTEENTH INTERNATIONAL MEDICAL CONGRESS AT BUDAPEST IN 1909.

The Fifteenth International Medical Congress, held in Lisbon, have chosen Budapest, the capital and residence of Hungary, for the site of their next assembly, and the preliminaries are already in process.

His Imperial and Apostolic Royal Majesty the King has graciously taken upon himself the patronage of the ensuing congress. The state and town have each contributed 100,000 crowns to defray the expenses.

The committee for the organization, execution, disbursements, and reception, as also for the sections is already formed and the statutes are drawn up.

There are 21 sections, each branch of science having a separate section assigned to it.

The date of the opening is fixed for August 29, 1909, and the sessions will be continued till September 4.

There is every reason to presume that the congress will be well attended. Hitherto they have shown an attendance of from 3000 to 8000 participants. Judging from the geographical situation of Budapest, at least from 4000 to 5000 participants may safely be reckoned upon.

The managers, of course, attach the utmost importance to the scientific activity of the congress, and every effort is being made to win over the most prominent representatives of medical science.

The first circular, which will contain every necessary information as well as the statutes, will be ready for circulation in the course of the year 1907. Meanwhile the Secretary-general of the congress (Sixteenth International Medical Congress, Budapest, Hungary, VIII, Esterházy-utcza 7), will have much pleasure in giving information to inquirers.

NOTES ON NEW BOOKS.

The Abdominal and Pelvic Brain with Automatic Visceral Ganglia. By Byron Robinson, M. D. (*Hammond, Indiana: Published by Frank S. Betz, 1907.*)

The present volume contains views concerning the anatomy, physiology, and pathology of the "abdominal and pelvic brain," the former consisting of the solar and epigastric plexus and the latter of the cervico-uterine ganglia located in each side of the uterus.

It is practically a treatise on the abdominal sympathetic nerves, a résumé of views which the author has discussed in current medical literature for a decade and a half. The author states that "a portion of this book entitled, 'Abdominal Brain and Automatic Visceral Ganglia,' was published in 1899 by the Clinic Publishing Company, the copies of which were exhausted in 1904." Portions of this book have also appeared in medical journals such as the Medical Review of Reviews, Medical Age, Medical Brief, Milwaukee Medical Journal, Medical Fortnightly, Medical Review, Medical Record, Medical Standard, Physician and Times, Columbus Medical Journal, American Medical Compend, St. Paul Medical Journal, Central States Medical Monthly, and Mobile Medical and Surgical Journal.

To those who are familiar with the above-mentioned book, "Abdominal Brain and Automatic Visceral Ganglia," or the numerous writings of the author in the above-mentioned journals, this present volume needs no introduction; and those who have enjoyed these contributions may be pleased to know that they may now find them collected and thoroughly revised in the present contribution.

The book consists of 671 pages and 207 illustrations by the artist Zan. D. Klopper. There are forty chapters, including one on "Shock," by Dr. Lucy Waite.

Each chapter is complete, in itself, on the subject of which it treats, and this has led to unavoidable repetition both in text and illustration.

It is impossible to give a résumé of the various subjects treated in so many chapters, and if one wishes to become acquainted with them, they must be read. This volume is in keeping with the other works of the writer, such as "Landmarks in Gynecology" and "The Peritoneum, its Histology and Physiology."

The American Illustrated Medical Dictionary. By W. A. Newman Dorland, A. M., M. D. 4th edition, revised and enlarged. (*Philadelphia and London: W. B. Saunders Company, 1906.*)

In size and general appearance this new edition of Dorland's dictionary resembles closely Gould's The Practitioner's Medical Dictionary, which has appeared recently. Although there are fewer pages in Dorland's work, the page is a little larger, so that probably the number of words in both is about equal, but Dorland's is somewhat the heavier, and, therefore, less easy to handle. It opens readily at any page like Gould's, and the type is almost the same. As a product of Saunders Company's press it is excellent, and to be recommended as one of the best medical dictionaries. This last edition contains 2000 more words than its predecessor, and six additional colored plates. That a new edition has been called for, shows the popularity of this book which is entirely justified in every respect. An English medical dictionary to equal the French work of Littré has yet to be written, however.

R. N.

Morat (J. P.) Physiology of the Nervous System. Authorized English edition. Translated and edited by H. W. Syers, M. A., M. D. (Cantab.). With 263 illustrations (66 in colors). pp. i-xxviii and 1-680. (*Chicago: W. T. Keener & Co., 1906.*)

This volume, a portion of Morat and Doyen's Treatise on Physiology published separately, deals with the functions of the nervous system. The book is a noteworthy addition to neurological bibliography and deserves and, we doubt not, will receive a warm welcome.

After a few introductory pages in which innervation in general is discussed and the relations of sensibility to energy, determinism, organization, and excitability, respectively, are referred to, the author gives the clue to the plan of his book and the basis upon which he subdivides his materials. In the nervous tissues, though they are composed primarily of cells, the interrelations of the cells is such that a genuine systematization is displayed. The study of the physiology of the nervous system may, therefore, be prosecuted from two points of view: "one, in which the functions common to all its elements are considered (*cellular functions*); the other, in which the functions special to the groups or systems formed by these elements are taken into account (*systematic functions*)." Morat, therefore, divides the contents of the book into two great parts: I, Elementary Nervous Functions; and II, Elementary Systematic Functions. Since the author adopts the neurone doctrine, fully making, as is the custom of American writers, *nerve-cell* (including all its parts) and *neurone* identical terms, his subdivision is the equivalent of a subdivision into I, The General Functions of Neurones, and II, The Functions of Neurone-Systems.

In the first part of his treatise, after distinguishing between the static or anatomical unit (the neurone) and the dynamic or physiological unit (the elementary nervous irritability, or aggregation of energies originating in the neurone), the writer plunges into his subject-matter proper and in the first chapter discusses "The Nervous Element" (anatomical data, dynamic condition, stimulation of the nerves, laws of electrical stimulation); in the second chapter he develops the doctrine of the "Energies of the Nerve."

In the second part, which is much the larger, there are two sections. The first section deals with Nervous Organization. There are four chapters in the section: (1) Sensibility and Movement; their Relations; (2) Primary Systematizations (Reflexes); (3) Consciousness and Unconsciousness; and (4) Superior Systematizations (Orientation and Equilibrium, Emotions, Intelligence, Cerebral Localizations). The second section deals with Specific Innervations, in five chapters: (1) Tactile Innervation; (2) Visual Innervation; (3) Auditory Innervation; (4) Olfactory and Gustatory Innervations; (5) Language and Ideation.

The matter is too extensive to lend itself well to brief critical review. The author has made an excellent book, and one which every working neurologist should be glad to have at his elbow. There are some defects one would like to see corrected, as for instances, (1) an apparent lack of familiarity with the newer work on heart-block in evidence in the chapter on innervation of the heart and (2) the sections dealing with motor localization in the cortex.

The author is to be congratulated upon his valuation of psychological work for cerebral physiology and one can only lament that he has not gone even farther than he has in this direction. He might well have brought in more of the results reached by his countrymen Ribot, Binel, and Janet.

The translator has not had an easy task but on the whole he has performed it well. The style is pleasing and dignified. An occasional split infinitive has crept in and here and there a misprint (e. g. Munck for Munk) mars a page, but these are trifling errors nearly always discoverable in a first edition. The thanks of English and American neurologists are due the publishers for

undertaking the issuance of a book which is more likely to help science than to increase their bank account. L. F. B.

The Treatment of Syphilis. By ALFRED FOURNIER. English Translation by C. F. MARSHALL. (*London and New York: Rebman Company, 1906.*)

The English translator has done justice to this classical work and it is, even in the new tongue, charming reading. One is tempted, indeed, after reading Gallic treatises, to suggest that a division of labor according to which the Germans made and recorded observations, the English drew deductions and the French wrote the text-books, would be a wise one. Fournier has, however, done more than write a crisp and entertaining text-book; he has brought to his task an enormous experience with syphilis and an unusual ability for analyses and clinical interpretation; furthermore, he has had all the problems of syphilis, social as well as medical, on his mind and has thought about them to good purpose. For these reasons, this book is one of definite value; that it is one of the books every medical student should have read, is hardly too much to say. In rendering it available for English physicians Dr. Marshall has not avoided all the pitfalls. On the whole, the book reads well; but one notices here and there the roughness of literal translation where accuracy could have been preserved and attractiveness enhanced by a legitimate freedom. The translator's persistency in having every "*mais*" represented by an English "*but*" is an example of conscientiousness at the expense of charm.

There are probably not more typographical errors than should be expected in a second edition. One notices, among others, "suphurous acid" (p. 92) and the "serious" nasal discharge of iodism in contradistinction to the muco-purulent discharge of coryza.

Introduction to Infectious and Parasitic Diseases Including Their Cause and Manner of Transmission. By MILLARD LANGFIELD, A. B., M. B., etc. (*Philadelphia: P. Blakiston's Son & Co., 1907.*)

The author states in his preface that "formerly this book was written for the use of nurses," but the original design was somewhat altered, so as to embrace both physicians and students of medicine, and the following sentences from the Introductory Note by Lewellys F. Barker, Professor of Medicine at the Johns Hopkins University, are sufficient to indicate the worth of this book. He says: "I have had the opportunity of reading the chapters before they went to press, and have no hesitation in recommending the book to the class of readers for which it is intended. The presentation is simple and clear and the author has carefully avoided the use of terms and the discussion of questions which would be unintelligible to beginners in the subject."

The book is divided into ten chapters on the Cause of Disease Bacteriology, Phenomena of Infections, Inflammation, Animal Parasites, Avenues of Exit (2), and Portals of Entry (2), Disinfectants and Disinfection, Collection and Examinations of Secretions and Excretions, with an appendix, a good index, and thirty-three illustrations. It is well printed and will undoubtedly prove of use to many who do not desire more profound knowledge of the subjects treated. R. N.

A Text-Book of the Practice of Medicine. By HOBART AMORY HARE, M. D., B. Sc., Professor of Therapeutics in the Jefferson Medical College of Philadelphia, etc. Second edition, revised and enlarged. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

The well-known name and writings of the author both in therapeutics and internal medicine insure the favorable reception of this volume. The arrangement and classification of the diseases is very good, although much the same as that used in other works of a similar character. In treating each disease separately the author has been most consistent in the arrangement of his subject-matter, using a very logical order throughout.

In regard to the reading matter, in the main it is more or less a facsimile of other books of the same character. Although the pathology of some diseases is very full and complete in others much has been left to be desired. On the other hand, the symptomatology and treatment are presented on the whole in a clear and thorough manner. But as the author states in his preface, "Much information that might be included, which deals with subjects which are still uncertain and debatable, has been excluded." Although this is a very laudable aim of the author, yet there are some instances where a more exhaustive discussion of these "uncertain" subjects might have done much to help the student grasp the characteristics of disease.

The chapters on Tropical Diseases are excellent for a book of this kind where the student and practitioner will find sufficient information to help him recognize rare conditions. In dealing with the diseases of the Nervous System the charts and illustrations employed are excellent, going far to establish a clear understanding of the pathology and symptomatology.

From a statistical point of view much material has been brought forward in a very clear and easily assimilable form. This is especially true in the acute infectious diseases as scarlet fever, diphtheria, and acute pneumonia.

The printing and binding are good and may be said to be somewhat above the ordinary. In fact, the present volume of this work is a worthy successor of the first edition. And it should take a prominent position amongst books of a similar class, in which there are so few better and many worse. J. C. M.

Clinical Diagnosis. A Text-Book of Clinical Microscopy and Clinical Chemistry for Medical Students, Laboratory Workers, and Practitioners of Medicine. By CHARLES PHILLIPS EMERSON, A. B., M. D., Resident Physician, The Johns Hopkins Hospital; Associate in Medicine, The Johns Hopkins University. (*Philadelphia and London: J. B. Lippincott Company.*)

This valuable volume deals with the systematic study of the sputum, urine, stomach contents, fæces, blood, and the various body fluids in the order named. There is a short introduction by Dr. Osler, who emphasizes the great importance of every medical student and practitioner being familiar with clinical laboratory methods and with their practical application in the study of disease at the bedside. Emphasis is also placed on the importance of a well-organized clinical laboratory as a part of the necessary equipment of a modern hospital and medical school.

There is more originality manifested by Dr. Emerson in the preparation of this book than has been shown by any other writer of a volume dealing with the same subject-matter that has appeared in recent years. This is particularly well shown in the illustrations, nearly all of which were made by a competent artist from observations personally made by the author in the wards or during class demonstrations in the clinical laboratory. It is rather refreshing not to find the hackneyed illustrations that have long served the purpose of the writers of similar works.

In a volume, all the sections of which are of such a high order, it is difficult for one to individualize. In the opinion of the reviewer, however, the section on the urine is preëminently the best. This would be expected naturally from one who has had such a good chemical training, and who has done such good work in the study of metabolism.

Early reviews of books are usually desired both by the author and publisher. Most books are reviewed before they have stood the test of time and experience. This is not true in the case of the present review. Sufficient time has elapsed, since the appear-

ance of the volume several months ago, for it to have been subjected to the best possible test, namely that of practical use. No similar work in recent years has stood the test so well. The author has wisely refrained from including numerous methods, chemical or otherwise, which are too often given in similar treatises, and which are of little practical value. The volume is essentially practical, and is invaluable to the student or practitioner.

Stöhr's Histology; arranged upon an embryological basis. By Dr. Frederick F. Lewis. The sixth American edition; from the twelfth German edition. (*Philadelphia: P. Blakiston's Son & Company, 1906.*)

Great credit is due an author or translator who first attempts to fill a need in the teaching of some subject, and a text-book which fills this need should not fail of a hearty welcome. In the translation before us we have such an attempt. The original text has been modified and amplified by the translator in order to "arrange the book upon an embryological plan." To accomplish this commendable purpose, the translator has given a clear but very brief outline of the development of most tissues and organs before considering their histological structure. The developmental summaries are occasionally further supplemented by a short description of the gross anatomy of the adult organs.

For presenting the subject of histology from an embryological standpoint the translator deserves the gratitude of teachers of histology. However, as to how far a mere summary of the developmental history of organs can acquaint the student or the physician without previous training in embryology, "with the developmental possibilities of their constituent tissues" is a matter of individual opinion. Since the translator does not intend at all to displace text-books in embryology, it is only fair to assume that the student and the physician will be prompted to refer to these by the translator's praiseworthy presentation of the subject of histology.

As to how faithfully the translation represents the twelfth German edition of Stöhr we must let the introductory note of the German author indicate, since the last German edition is not at our disposal for comparison. It is clear, however, that we have before us a composite of two ideals of a text-book of histology, and we do not doubt that the translator's ideal would have found fuller realization in a text-book written entirely by himself.

We regret that matters which are still *sub judice* are occasionally presented in a dogmatic way and that references to articles have not been substituted for, or added to, those of individual investigators. The former would tend to cultivate the proper attitude of mind on the part of the student towards scientific problems, while the latter would encourage him to consult the literature on subjects still under discussion.

The volume is divided into two parts. The first part is composed of three chapters on microscopic anatomy, and the second part of twenty pages contains directions for the examination and preparation of tissues and the use of the microscope. In the three chapters of the first part, the subjects of the cell, the tissues and the histology of the various organs are discussed in the manner indicated above. The text is clear throughout and without the obscurities so apt to characterize translations. The BNA is used consistenly, though Latin and English terms are frequently used in the same sentence. Examples of this are: p. 280, ductus ejaculatorii and seminal vesicles; p. 322, bulbus and bulb. The hyphen, too, has been used rather inconsistently as the following instances illustrate: p. 100, intercellular, inter-fibrillar; p. 106, knob-like, semifluid; p. 126, thick walled; p. 128, rod shaped; p. 133, text-books; p. 142, bell shaped; p. 148, well defined; p. 162, thin walled; p. 263, inpocketing; p. 266, out-pocketing; p. 284, C shaped; p. 285, outpocketing; p. 297, mucus-producing; p. 298, kerato-hyalin; p. 316, keratohyalin; p. 330, funnel shaped; p. 331, interrenal; p. 332, well fixed; p. 333, long-meshed; etc. Some of these obviously are typographical errors. It may also be noted that since both the English and metric systems of measurement are used in the text, such an abbreviation as *gr.*, for example (p. 410), is uncertain for the beginner since it usually stands for grain and not for gram.

As a piece of bookmaking, the volume compares very favorably with current American text-books. The type is excellent, the illustrations good and numerous, and the diagrams which supplement them usually clear and well-conceived. The legends are printed in differential type and consequently easy to use, and the index is carefully made. The interpolated parenthetical words and remarks are of much value to the student, save where they convey such useless fancies as that of Holmes, to the effect that the sudoriparous glands resemble a fairy's intestine. This figure may be considered of doubtful value and probably transcends the imaginative power of most students—and histologists. We refer students to the wise words of Sir Benjamin Brodie and John Tyndall upon the scientific use of the imagination. The typographical errors are few. The following may be noted: Fig. 26, *de;* Fig. 32, omission of (a); p. 39, connectve; p. 90, know(n); p. 163, civinity; Fig. 425, areria, and p. 499, *is* for *it*. Attention may also be directed to the following phrases: p. 157, lymphatic vessels . . . . become involved in the lymph sinus; p. 187, parotid gland is an organic gland; p. 279, honeycombed with folds; p. 308, umbilical cord is a pearly rope of tissue; p. 402, wash for an hour or a few days; p. 408, slides rubbed with albumen; and to the fact that the percentages of alcohol as given on pp. 401 and 403 are only approximate.

These matters of textual criticism should be regarded as purely subordinate, however, and do not seriously affect the value of a well-written text-book with copious, clear illustrations, presenting the main facts of the subject of histology from an embryological standpoint. A. W. M.

A Treatise on the Principles and Practice of Medicine. By Arthur E. Edwards, M. D., Professor of the Principles and Practice of Medicine and of Clinical Medicine, in the North Western Medical School, Chicago, etc. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

Probably the feature that impresses one most strongly in going over this work is the immense amount of detailed information which the author has collected. Throughout the work he has apparently made the effort to bring together the fullest information on various points rather than to attempt to give a more or less general picture. We are all familiar with the difficulty in teaching which comes from the tendency of the student to always associate a certain picture with a special disease. Doubtless the method which Dr. Edwards has pursued will tend to neutralize this, but of course the best method is for the student to learn the clinical features from the patient.

On the whole, it may be said that Dr. Edwards has written a very satisfactory text-book. Certainly the careful way in which he has studied the literature makes the articles especially useful for teachers and practitioners. He has added a great many historical notes which add to the interest. Necessarily these are brief, but appeal strongly to those of us who are interested in the historical side. There are some of these, however, to which exception may be taken. Thus, it is hardly correct to say that typhoid fever was first recognized by Louis. He drew special attention to the fact that in a certain group of continued fevers there was ulceration of the bowel, just as Bright and others had done, but this can hardly be termed the recognition of the disease. Nor is it correct to say that Brettoneau first noticed specific changes in the intestines in typhoid fever. The essential lesions

in the bowel had been noted long before his day, and he did not separate them from those of enteritis. There is some discrepancy in the note of the discovery of choroidal tubercles in tuberculous meningitis, which is probably an oversight. On page 316 it is stated that they were "first found at autopsy by Nanz (1857), Nusch and Cohnheim, and clinically by von Graefe (1857), and Leber," while on page 1051, it is said that they "were first found anatomically by Autenrieth (1808), and Guéneau de Mussy (1837), and clinically by Jäger, Manz, and Busch."

The sections on the symptoms and physical signs are especially good. In many of these the number of facts and statistics grounded together is really remarkable. This is well seen, for instance, in the section on aneurism of the thoracic aorta. This feature will render it especially useful as a work of reference. The author's sections on treatment are to be fully commended, and measures other than giving of drugs receive proper attention.

The section on the diseases of the nervous system seems to be very well done. It is rather difficult to understand why cerebrospinal meningitis is placed here and it would seem better among the infectious diseases. We question whether the physicians in the South would agree that neurasthenia is more common in northern climates. It is perhaps difficult to give exact figures, but judging from experience here, it is *by no means rare* south of Mason and Dixons line.

There are, however, a good many points in which we should suggest improvement. There are those who do not think that attention to form in medical writing is worthy of any special attention. Many of us, however, are in agreement with Professor Allbutt in his plea for more care in writing, even if we can only follow him afar off. Thus, we find that "a certain per cent of unoperated cases die." Is it not the patients who die and not the cases? Then again, comes the expression "successfully operated," which would sound better if another word was added. It seems as if the plea for the proper use of the term rheumatism needed to be repeated when we find a new text-book of medicine speaking of "gonorrheal rheumatism" and also of "scarlet rheumatism." In association with arthritis there is some doubt of the correctness of the view that chronic follows acute rheumatism. In the description of arthritis deformans we should not agree with the author that the acute type is uncommon; it is frequently unrecognized.

While we have dwelt on many of the points that might be improved, it must not be thought the general verdict of this work is other than a favorable one. Dr. Edwards has given us a good text-book. We only wish to point out how the good may be made better. The publishers have done their part well in giving a clear page.

A Treatise on Orthopedic Surgery. By ROYAL WHITMAN, M. D., etc. Third edition, revised and enlarged. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

The general plan of the third edition of Whitman's Orthopedic Surgery does not differ from its immediate predecessor. The scope of the book has been somewhat widened in order to take up more fully those subjects which have recently claimed attention in orthopedic literature. The pathology and treatment of certain affections have been amplified. The chapter on "Fracture of the Neck of the Femur" has been rewritten and profusely illustrated, and the author has forged into the preventive medicine by pointing out the possibilities of preventing deformities as well as of curing them.

Evidently much thought has been given to the selection of illustrations, which clearly point out the pathology and treatment of the subject considered.

The arrangement of the book is excellent. The subject is presented in a logical and concise manner. Numerous illustrations make it exceedingly valuable as a text-book for those students taking up the subject of Orthopedic Surgery. One feels that he is given the experience of a teacher who has thoroughly digested the material of a large orthopedic clinic, and has given each subject the consideration which its importance demands.

W. T. BAER.

Progressive Medicine. Vol. II. June, 1907. Edited by HOBART AMORY HARE, M. D., etc., assisted by H. R. M. LANDIS, M. D., etc. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

This digest of "advances, discoveries, and improvements in the medical and surgical sciences" is published quarterly, and is valued by the medical profession because it keeps them well informed of the new work that is being done constantly in all countries. The contributors are men of note in their own lines, and the work is edited in such a manner that it is easy to find the latest information on any branch of medicine or surgery. This volume is devoted to hernia, surgery of the abdomen, gynæcology, diseases of the blood, diatetic and metabolic diseases, diseases of the spleen, thyroid gland and lymphatic system, and ophthalmology. The contributors of the articles are W. B. Coley, E. M. Foote, J. G. Clark, A. Stengel, and C. Jackson. As a work of the publishers, the volume is to be commended, but it would seem as though often the illustrations might be better chosen, and better reproduced.

R. N.

A Treatise on Surgery. By GEORGE RYERSON FOWLER, M. D. Vol. II. (*Philadelphia and London: W. Saunders Company, 1906.*)

This volume belongs to the already large, and daily growing, class of copiously illustrated text-books of surgery. There is about it nothing striking; the arrangement and general treatment of the material are conventional—as, indeed, they must needs be; but a moderately high average is maintained throughout and one misses that lack of balance seen in Systems of Surgery in which certain articles, written by careful and thorough men, are excellent and others, written to fill up space, are wretched. One is struck by the author's wide acquaintance with the literature; the pages are studded with the names of those who have made contributions to surgery; and this extensive review of the field adds value to the book.

Most of the pictures are good; some are excellent; a few are bad. The conventional illustrations have been included, as for example, the views of the various stages of catheterization, though the very important maneuver of putting the assisting hand in the perineum is, as usual, omitted.

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ON THE TEACHING OF PATHOLOGICAL PHYSIOLOGY.

II.

By W. G. MacCallum, M. D.,

Associate Professor of Pathology, Johns Hopkins University, Baltimore.

During the autumn term of the past year there was given the second part of a course on Pathological Physiology, the first part of which was carried out during the autumn of 1905 and described briefly in the August number of this journal for 1906. It is my desire to give here a short outline of the work done in this second part of the course and to endeavor to make clear the importance of teaching by experiments and demonstrations the nature of the functional disturbances which constitute the conditions met with by the practising physician and the hospital interne. It may not be amiss to repeat some of the arguments which were put forward in that previous paper with regard to the advantages of approaching the subject of disease from this point of view, for we are anxious that such teaching should spread further than it has already done in this country.

Since the time of Morgagni every student of medicine has

found in the anatomical changes in the organs the basis for his explanation of the symptoms of disease. He studies the phenomena of the disease and then, either with the tissues in his hands at autopsy or by referring to his autopsy experience of similar cases, he explains the sequence of these phenomena upon anatomical changes. This differs very little from an experiment in which he produces an anatomical change and watches the effect, except that here he must wait for the autopsy to learn precisely what Nature's experiment has been. Thus, the clinician is undoubtedly a pathological physiologist using as his subjects the human beings who are sick. Certain methods of planned experimentation he can apply to these patients to learn something of the character of the changes he is watching, far more indeed than was in the power of the doctors of old, but even yet there are limits which he must observe out of respect for the comfort of the patient and for other reasons, which make his observations in some respects necessarily indefinite and inexact. Pathological physiology in this sense, is thus the very oldest branch of medicine—for centuries while anatomy and the rest were obscure untrodden paths physicians have been watching night and day without pause the phenomena of disease and pondering upon their nature, testing as they could, with finger on the pulse or with sensitive hand on the hot brow of the patient, the progress of the changes and making surmises as to their outcome.

In modern times the post-mortem study of the anatomical changes that really had been going on has made these tests of greater value since it has become possible by the aid of such experience to interpret their results. Great strides have been made, too, in the perfection of the tests themselves, and all sorts of instruments, devised for the purpose of measuring and studying minutely the functional disturbances, now place the clinical methods of diagnosis and study almost on a level with the methods of the physiologist. Not quite, however, for the physiologist is not limited by consideration for the welfare of his subject in making his investigation and he can apply any method of study that he is ingenious enough to devise. While the clinician may take a tracing of the pulse or even of the heart-beat with a suitable instrument, the physiologist can insert canulas directly into each chamber of the heart and record its activities with as many manometers. The clinician may study the stools and theorize as to the character of the disturbance in the pancreas, while the physiologist may bring out the gland to the surface, establish a pancreatic fistula, and continuously study the chemical character and function of the pancreatic juices.

In teaching clinical medicine these gaps in first-hand knowledge are usually made up by the application of the knowledge which the physiologist has gained from normal cases to the pathological conditions which are found at autopsy or indicated by the methods of clinical diagnosis, but as a rule the student cannot make as minute and detailed study of the actually progressing disturbance of function as he must desire to make.

Hence the teaching of pathological physiology in an experimental way; it is nothing more nor less than clinical medicine with greater opportunities for studying the patients. Its aim is to reproduce experimentally the diseased conditions which one sees in the wards, to modify these diseased conditions in various ways, observing the corresponding alteration in the symptoms, and to observe directly with the eyes, the ears, with every possible instrument of precision applied directly, the intimate nature of the altered functional activity. The physiologist is supposed to study normal functional activities. This is the equally intimate study of disturbed or altered functional activity in a diseased organ.

It is a part of pathology co-ordinate with pathological anatomy and with pathological chemistry. No study of disease is complete with the study of its pathological anatomy without any notice of the alterations in the chemical nature of the tissues and fluids involved, nor is it complete without any observation of the disturbances of function which result.

For these general reasons it has seemed imperative that we should teach something of this disturbance of function, using methods as accurate as possible, and bringing the actual disordered functional process before the eyes of the student as he might watch a laboring engine with a broken cog in its wheels. This rather than leave him to reconstruct from his vaguely remembered pathological anatomy the probable explanation of the symptoms which he views from a respectful distance.

The course in pathological physiology was planned, then, with the idea of teaching in the laboratory of experimental pathology the nature of alterations of function in a way quite analogous to that in which the alterations of anatomical structure are taught in the laboratory of pathological anatomy. Facilities for this are afforded, as described in the previous paper, in the Hunterian Laboratory; and the course was arranged in such a way that each year the diseases of one group of organs might be studied, since it was thought that this would be more satisfactory than an attempt to cover superficially, each year, the disturbances of function of all the organs. Accordingly, the circulatory system formed the first subject and the results of that work were described in the paper referred to. The second division of the course which has been carried out this year was concerned with the diseases of the organs of internal secretion and an outline of this may be given here.

Some difficulties were encountered in this course owing to the fact that it is impossible to bring about symptoms very quickly by disturbing certain of these glands, and in such cases the graphic results which could be brought before the students in connection with lesions of the circulatory apparatus were not to be looked for; nevertheless it was generally possible to perform the necessary operation with the aid of a

portion of the class and to present the result at a succeeding meeting of the whole class. On the other hand, certain organs, such as the hypophysis, proved in our hands to be almost entirely inaccessible, at least as far as class demonstrations go.

The work in this instance was not, however, entirely experimental, for in the case of the organs of internal secretion the embryology, comparative anatomy, and pathological anatomy are subjects of such extreme interest that we spent some time in discussing those things, and on the other hand the class was taken into the wards of the hospital to observe such cases as illustrated the effects of disease of these glands. It is often possible in that way, of course, to show a picture of disease which could not be produced experimentally in animals within the time allotted to the course.

The adrenals, pancreas, hypophysis, cells of Leydig, thyroid, and parathyroid formed the chief subjects of discussion, but some attention was also directed to such structures as the corpora lutea, the carotid and coccygeal glands, the thymus, etc.

The adrenal was first taken up and studied with regard to its embryological development in several animals, but although the specimens from the lower animals are very instructive the series of human embryos which form Dr. Mall's collection gave us especially valuable information. The inwandering of the medullary elements into the solid mass of the cortex could be well traced and the development of the chromaffine reaction in later life easily demonstrated by fixation in the appropriate fluids.

Extirpation of the adrenals was shown to be followed by extremely grave symptoms, perhaps resembling those of Addison's disease in a greatly exaggerated form, but leading so rapidly to complete apathy and the death of the animal, that no good comparison could be made; such results appeared far less rapidly in rats, in which it is shown that there are frequently accessory adrenals. Efforts at determining whether this might be the result of the loss of an antitoxic organ were made by removing a large part of the blood and replacing it by a larger amount of salt solution, but although this diluting process seemed to resuscitate one animal, subsequent experiments which will be detailed separately threw much doubt on that conclusion. The blood removed when injected into a normal dog did produce an illness which lasted 24 hours, but from which complete recovery occurred. No blood-pressure elevating effect such as is produced by the extract of the gland could be obtained by means of the blood removed from the adrenal vein, even though a considerable quantity was thus obtained. Indeed it could hardly be expected that there should be enough blood-pressure raising material in the blood passing through the veins of an adrenal within a few minutes to produce any marked effect upon a normal dog.

The anatomical studies of the adrenals from various autopsies showed that in some cases very extensive destruction of the adrenals had occurred without Addison's disease, while it is well known that in some cases of Addison's disease the adrenals show no very apparent lesion. Interest, therefore, attaches to the minute study of the entire chromaffine system, including all the sympathetic ganglia and the carotid bodies in cases of Addison's disease in order that Wiesel's theory that the disease is dependent upon the destruction of all the chromaffine tissue may be proven or disproven.

The carotid bodies were studied anatomically and embryologically and were extirpated from a dog; no definite result followed this experiment, however, and the dog recovered entirely.

At this time a remarkable case of acromegaly appeared in the hospital, and the class was taken to the wards to study him. In connection with this the anatomical changes exhibited by a previous case which had come to autopsy were demonstrated, and the relations which the hypophysis cerebri bear to acromegaly discussed. Attempts to repeat the operation described by Friedmann and Maas for the extirpation of the hypophysis were unsuccessful and have not since been repeated, but it is proposed to carry out such experiments during the year.

The pancreas was studied only in so far as it has to do with diabetes; and the development, histology, and pathological changes in the islands of Langerhans, and in the pancreas in general, were considered in this relation. The form of diabetes produced by the extirpation of the pancreas was studied in detail. It was found that intense glycosuria appeared half an hour after the extirpation of the gland, the maximum amount of sugar being reached only after three or four hours. The sugar was present at times to the extent of 5 per cent. At no time, however, was it possible to demonstrate the presence of any of the series of acetone bodies, although in several cases they were tested for carefully.

On the chance that the control of carbohydrate metabolism might be restored by the replacement of pancreatic substance a quantity of emulsion of pancreas was injected into the peritoneal cavity after the extirpation of the pancreas had been completed for several days. No definite change in the glycosuria was thus produced however. Partial extirpation was shown to have no effect as far as the production of glycosuria goes, even when by far the greater part of the gland is removed, leaving only that portion which is attached to the intestine. Interesting material for the study of regeneration of the pancreas was furnished by these experiments. In other cases the ligature of the duct of part of the pancreas or even of the ducts near the intestine, cutting off the whole pancreas from secreting into the intestine, was not followed by diabetes. The portion of the tail of the pancreas separated by the ligature from the rest, did, however, in the well-known way, undergo an extreme atrophy, the islands of Langerhans alone remaining well preserved.

The interstitial cells of Leydig in the testicle were studied under various conditions anatomically and embryologically and experiments are still under way in the hands of one of the students, with the aim of determining the effects of ligation

of the vas deferens, of replacing the testicle in the abdomen, etc. The experiments tend to show that these cells are independent of the spermatogenic tissues and interest centers on their relation to the development and maintenance of the secondary sexual characters. Similarly, the rôle of the corpora lutea was discussed in the light of Fraenkel's work on the subject and in one case of early pregnancy in a dog a corpus luteum was excised from each ovary; no others could be seen. The dog recovered perfectly, and no further signs of the pregnancy were to be observed. Still such an experiment is by no means conclusive and only a very large series can definitely establish the relations which Fraenkel claims hold good.

In the case of the parathyroid, study of the anatomical and embryological relations were made, after which the effect of ablation of the glands was shown. Tetany develops with great regularity in dogs after the extirpation of four parathyroid glands and in this case it was characteristic. The infusion of a quantity of salt solution into the vein after bleeding abolished the symptoms of tetany completely for a period of several days. It was further shown that emulsion of the parathyroid gland injected into the veins would also cure the well-developed tetany.

One case came to our notice in another hospital, in which the thyroid with most of the parathyroid tissue was removed from a little girl. Violent tetany developed after three days but was relieved by the subcutaneous injection of an emulsion of the parathyroids of the cow. Evidently enough parathyroid tissue remained to carry on the function; for after two such attacks had been treated in this way, the symptoms returned no more and the child has apparently recovered completely. It remains to be seen whether some special strain such as pregnancy or lactation will bring about the tetany again from parathyroid insufficiency.

Extirpation of the whole of both thyroid lobes leaving the parathyroid which was at the upper pole of each resulted in no tetany, and the dog lived in perfect health for several months, when he died of pneumonia. At the autopsy several masses of thyroid tissue had developed about the trachea, and beneath the arch of the aorta. These were very small, about the size of a pea at most, and all together would not equal in bulk one of the thyroid lobes. Histologically they show the characters described by Dr. Halsted, in compensatory hypertrophy of the gland. It is apparently impossible to produce myxœdema in such an animal as the dog, on account of the presence of these accessory thyroids, which are so small and in part so inaccessible, as to be quite invisible at the time of the extirpation of the main gland, but which then hypertrophy to meet the demand for thyroid tissue.

Experiments on the effect of extirpation of the thyroid and of the thyroid and parathyroid together in sheep and goats will be detailed separately. The anatomical conditions, as is well known, differ greatly from those in the dog, and the complete extirpation of the parathyroids usually involves the destruction of the thyroid, since one parathyroid on each side is deeply embedded in the thyroid. As a rule the symptoms following such extirpation were slight or not noticed at all, but in two goats we succeeded in producing violent tetany which agreed closely with that seen in dogs.

Cases of goitre and exophthalmic goitre were studied by the class in the wards and the clinical signs correlated with the ideas previously obtained of the functions of the thyroid. One case of exophthalmic goitre was followed by the class until the operation, after which the extirpated thyroid was studied anatomically, the usual modifications of the gland being found while the parathyroid glands removed with the thyroid showed no alteration whatever.

At the time there were not as many cases of goitre in the hospital as usual, but whatever material was available was used; in lack of this the rich material of the pathological museum was demonstrated, illustrating goitre formation, and the chemical relations of the colloid substance in normal and diseased thyroids discussed. The dependence of the growth of goitres, whether of the diffuse colloid type, the adenomatous nodular type, or the exophthalmic type, upon these chemical relationships and the corresponding needs of the body were entered into and debated. One case in which myxœdema existed as the result of almost complete disappearance of the thyroid will be detailed in a separate paper. In this case the parathyroids were unchanged and their complete independence of the thyroid thus proven.

The work in connection with these organs has been continued by some of the students of the class; and papers follow on the anatomy and topography of the parathyroids in various animals used for experimentation, on the absence of any appreciable amount of iodine in those glands, on the production of tetany in herbivora by the extirpation of the parathyroids, etc.

Next year it is proposed to continue this course, taking up the study of the functional disturbances of the organs of respiration. The work is arranged in the new schedule especially for students of the fourth year, who may now, during one trimester, elect it as their major subject of study, when they will be required to devote three hours daily for eleven weeks to the experimental study of some problem, and if possible to present a thesis on that subject. Others who choose experimental pathological physiology as a minor elective subject will attend the demonstrations which are given twice weekly. The course is, however, open to all students who have a sufficient knowledge of the normal physiology and pathological anatomy of the organs studied.

Such a summary as this is published in this way in order to show the general character of the work which we are trying to promote in the system of medical education and in the frank endeavor to enlist the enthusiasm of others who may be able to put themselves in a position to teach pathology in this way.

THE RELATION OF IODINE TO THE PARATHYROID.

By W. L. Estes and A. B. Cecil.

(From the Hunterian Laboratory of Experimental Medicine. Johns Hopkins University.)

Subsequent to the discovery by Baumann of iodothyrine, the active principle of the thyroid gland, the possibility of the presence of an iodine containing compound in the parathyroid was first suggested by Gley (1). He carried out his investigations on rabbits and dogs, estimating the iodine of each thyroid and parathyroid of the same side. Baumann's method for detecting iodine was slightly deviated from; for, instead of making the combustion in a crucible with sodium hydroxide, a porcelain dish with the dried glands was introduced into a Bohemian glass tube at one end of which a current of oxygen was permitted to enter and at the other end was placed a vessel with 2 to 3 cc. of sodium hydroxide. After the combustion was completed the apparatus was washed with hot water and the solution used for the determination.

Gley thus found in the rabbit's parathyroid, absolutely 2.35 times as much iodine as in the thyroid and relatively 37 times as much; and in the dog the parathyroid contained absolutely less (about one-fifth) than the thyroid, but relatively it contained 16 times as much.

Gley, therefore, concludes that the parathyroid must play some part in the "Thyroid System of Organs," the parathyroids preparing the product of secretion which is then transferred in some way to the thyroid and finally utilized according to the demands of the organism (2).

Lafayette Mendel is widely misquoted as having found great quantities of iodine in the parathyroid. The paper to which reference is made, "On the Occurrence of Iodine in the Thymus and Thyroid Glands" (3), discusses the presence of iodine in accessory thyroids and the thymus, and not in the parathyroids, and in this connection Mendel refers to the presence of iodine in the spleen, adrenal, salivary glands, and makes casual mention of Gley's finding iodine in the parathyroid. It is his concluding statement that has probably been misconstrued: "Accessory thyroids in man may contain both relatively and absolutely more iodine than the thyroid proper of the same individual."

Jeandelize in discussing the chemistry of the parathyroid in his monograph (4) reaches a conclusion similar to that of Gley, believing not only in the "Thyroid System of Organs," but adding "That this hypothesis agrees very well with the physiological effects of extirpating the gland"; *i. e.,* he believes that the iodine is disseminated in the organism after having been stored in the thyroid and previously prepared for assimilation in the parathyroid. In case of parathyroidectomy the iodine is not properly prepared and the organism suffers acute intoxication. On the other hand, after thyroidectomy the storehouse and distributor of iodine no longer exists, no acute symptoms arise since the iodine has been purified in the parathyroid, but malnutrition is in evidence because the iodine is not distributed according to the demands of the organism.

Chenu and Morel (5) more recently have worked on chickens, dogs, and rabbits. They used in their determination equal weights of thyroid and parathyroid tissue and followed Baumann's method: potassium hydroxide for combustion and carbon disulphide for the color test. They were thus able to read to .0025 mgr. of iodine. In no case in which they examined the parathyroid of a single animal could they detect any iodine, although the same amount of thyroid from that animal was found to contain a quantity of iodine which could be estimated. When they combined the parathyroids of eight dogs they were able to demonstrate iodine (.0563 mgr. to 1 grm. of fresh parathyroid). They conclude therefore that the thyroid and parathyroid differ chemically and that the active principle of the parathyroid is not an iodine-containing compound.

At the suggestion of Dr. Wm. G. MacCallum we have repeated this investigation on the parathyroid of dogs, cows, horses, sheep, and man. Instead of taking a single parathyroid for a determination as hitherto, we have used many parathyroids, drying them as collected on glass plates at room temperature.

For analysis we have used Baumann's method as stated by Kocher, preferring to use chloroform rather than carbon disulphide for the colorimetric test. The dried glands were weighed and placed in an iodine free crucible with 5 cc. of water and 2 gr. of sodium hydroxide for every gram of the glands. This mixture was evaporated to dryness over a flame and ashed. Then an amount of potassium nitrate equal in weight to the amount of sodium hydroxide used was added, and the mass heated till it assumed a white appearance. The crucible was then cooled and treated with 20 cc. of water, then heated and the liquid filtered; the crucible and filter paper being thoroughly washed with hot water. The cooled filtrate was treated with 20 per cent sulphuric acid and shaken well with 5 cc. of chloroform. If iodine is present the chloroform assumes a pink tint.

Iodine may be determined quantitatively by a comparison of this color with that produced by a known quantity of a standard potassium iodide solution thoroughly shaken with 20 to 25 cc. of concentrated sodium sulphate, 10 to 12 drops of a 1 per cent solution of sodium nitrite, 3 to 5 cc. of sulphuric acid (20 per cent) and 5 cc. of chloroform. By careful manipulation the color produced in the chloroform by the unknown can be matched by the color produced by the known amount of potassium iodide; and thus the amount of iodine present is computed. Iodine to the amount of .0025 mg. could be detected.

The crucible used for each determination was tested for

iodine by running through the above process and noting whether a color with chloroform was produced or not, thus rendering it iodine free. Gentle heat was invariably found to produce the quickest and best results, easier filtering and clearer filtrate; iodine is also volatile under great heat.

The following are our results:

ANIMAL.	WT. OF DRIED GLANDS.	AMT. OF IODINE.
Dog	.25 grams.	Infinitesimal.
"	.24 "	"
Cow	5.00 "	Negative.
"	5.00 "	"
"	1.00 "	"
"	1.00 "	"
"	1.00 "	"
"	1.00 "	"
Horse	3.78 "	.06 mg.
"	.743 "	Negative.
"	1.135 "	"
Sheep	.2276 "	"
"	.225 "	"
Man	.87 "	"
"	.61 "	"
"	.3316 "	"
"	.26 "	"

It will be seen that though large quantities of parathyroids were used for each determination in but three instances was the slightest trace of iodine detected and this in such trifling amounts as to be insignificant in importance. To confirm our work from time to time control experiments were made by adding a small amount of potassium iodide to the dried glands. This mixture was then put through the process, and in every case the amount of iodine added could be computed by the colorimetric method.

It should be noted that especially in such an animal as the dog it is difficult to dissect out the parathyroid in such a way as to be certain that no thyroid tissue is included in the mass removed. In many cases this is true also of the human parathyroid and it seems probable that in those instances in which iodine was detected in the parathyroid material it may have been due to the accidental admixture with thyroid tissue.

These results are not markedly different from those of Chenu and Morel, who in reality found extremely minute quantities of iodine in the parathyroid, and though Gley's experiments stand so emphatically contrary to what we have found, yet in view of the wide field our experiments embrace we conclude:

(1) That iodine as a constituent of the parathyroid may, generally speaking, be neglected.

(2) That if present at all iodine occurs in such minute quantities as to be of no functional significance.

(3) We fail to find chemical grounds for the hypothesis of the thyroid system of organs.

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PANCREATIC ATROPHY IN A DOG FOLLOWING IMPACTION OF CALCULI IN THE DUCT.

By R. D. McCLURE,

(From the Hunterian Laboratory, Johns Hopkins Medical School.)

An interesting condition of the pancreas, produced by concretions in the duct of Wirsung was discovered in an autopsy on a dog in the Hunterian Laboratory. It is reported at the suggestion of Dr. MacCallum.

The pancreas was lying free from the surrounding tissues and was nowhere bound by adhesions. The tail presented a striking appearance. It was dark colored, curiously nodular and shrunken, and much smaller and firmer than the remaining portion of the pancreas. The total length was 15 cm. The shrunken tail measured only 2½ cm. and passed abruptly over into normal looking pancreas. On section the parenchyma of the head end was normal in consistency and appearance. The characteristic lobulation in the small amount of tissue of the shrunken end was entirely absent, being replaced by connective tissue in which minute bulgings could be made out.

The longer proximal portion of the duct was found to be normal and contained a grayish opalescent fluid. A probe passed through the papilla met no resistence and the lumen was patent as far as the shrunken portion where it suddenly became constricted, causing complete occlusion. The duct distal to the occlusion was greatly dilated and formed by far the greater portion of the shrunken mass. This cavity was distended by a thick grayish fluid. The search for the exciting cause of the constriction revealed two minute calculi, tightly impacted in the constricted lumen. These were small, round, slightly rough, opaque bodies, not larger than the head of a pin. Careful examination failed to reveal any more such

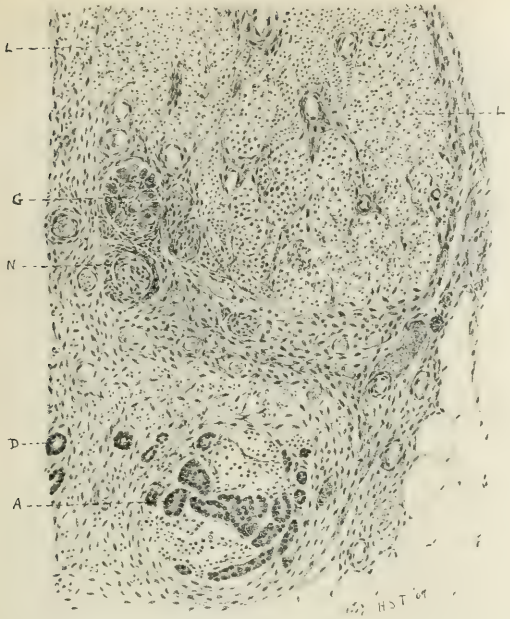


Fig. 1.—Portion of atrophied pancreas distal to obstruction of duct. *L*, degenerated parenchyma; *G*, ganglion with large nerve cells; *N*, nerve trunk; *D*, small branch of pancreatic duct; *A*, remnants of island of Langerhans.

bodies, either in the lumen of the duct or in the surrounding tissue.

With the kind assistance of Dr. Loevenhardt these concretions were analyzed and were found to be composed of calcium carbonate with only a trace of proteid.

The microscopical picture was an interesting one (Fig. 1). The parenchyma, islands, and ducts of the proximal end were normal in every particular. Distal to the constriction, at first glance the tissue would not be recognized as pancreas. The duct epithelium was degenerated and in many places desquamated. The surrounding tissue was largely composed of connective tissue in which were embedded large numbers of cells of the islands of Langerhans. These, however, did not appear normal and were no longer in columns as in the normal island, but were very irregularly arranged and widely separated, by connective tissue which invaded these areas.

Only a few remnants of the normal acini were present. These were far apart and entirely surrounded by connective tissue. The cells were degenerated and did not stain clearly.

The blood vessels were well filled with blood and many non-medullated nerves were seen in the section. In the accompanying drawing by Mr. Herbert S. Thomson a large ganglion is seen.

The small portion of pancreas affected was probably not great enough to alter in any way the metabolism of the dog, even if the Islands of Langerhans, too, had been entirely destroyed.

TETANY AFTER PARATHYROIDECTOMY IN HERBIVORA.

By W. G. MacCallum, M. D., H. S. Thomson, and James B. Murphy.

(From the Hunterian Laboratory, Johns Hopkins Medical School.)

The statement has been so generally made that no evil results follow the extirpation of the thyroid and parathyroids in herbivorous animals that it has seemed to us very remarkable at least, and worthy of investigation. The less toxic character of the decomposition products of the food of herbivora is usually assigned as the reason for this absence of tetany and the idea was even put forward in another way by Verstraeten and van der Linden who stated that after parathyroidectomy in dogs they could prevent the appearance of tetany if they fed the dogs on milk only. This is, however, not true as was shown by some of our experiments recorded in a previous paper.

We had the idea in approaching this investigation that previous workers had possibly overlooked some parathyroid tissue so that after the operation there still remained enough to prevent tetany. Indeed as will be seen from our results this idea is still in our minds after our own experience with sheep and goats. We did, it is true, find four parathyroids in every case very regularly situated in the thymus and thyroid, and the most painstaking and minute dissection of the remaining tissues at autopsy never revealed any further trace of parathyroid tissue, but still the suspicion remains that somewhere there is more of that tissue. In sheep and goats the distribution of the parathyroids is quite the same. There are two embedded or partly embedded in the thymus, one on each side at the level of the thyroid cartilage of the larynx and just in front of the carotid and vagus nerve. As is well known the thymus in these animals extends from the submaxillary gland down into the thorax, although it is not always quite continuous throughout this distance, and the parathyroid is quite easily distinguished as it lies in this pale cream colored tissue. After a little pulling aside of the lobes of the thymus it springs into view as a bright red rounded smooth body about 3-5 mm. in diameter. Its homogeneous appearance and red color render it easily distinguishable from the lymph nodes which are sometimes found scattered in the same tissue. It is quite sharply outlined and distinct from the thymus, but is apparently supplied with blood by a branch of one of the vessels supplying the thymus.

The thyroid consists of a rather small lobe on each side

united across the front of the trachea by a delicate band or isthmus. Embedded in each of these lobes is the remaining parathyroid. These masses which we have found in the thyroid in every case cannot be clearly seen in the living animals, and we have found it necessary in order to secure their extirpation to remove the whole thyroid lobe each time. In hardened tissue, however, they stand out fairly plainly on section from the surrounding thyroid tissue. They are not furnished with any capsule, but come into very intimate relation with the thyroid tissue. No very definite statement can be made as to their exact position in the thyroid because this seems to vary a good deal.

As noted above most diligent search has been made through the rest of the tissue of the head, neck, and thorax for any further parathyroid tissue, but without avail, although quite a number of animals have been thus carefully dissected.

Histologically the parathyroids of sheep and goats are practically not to be distinguished from one another. The tissue of that gland which is embedded in the thymus is quite identical with that of the intrathyroid gland, and on this ground it seems to us that the so-called parathymus gland of Schaper and others is undoubtedly merely the second parathyroid.

The glands are very compact and very vascular. The cells are apparently all of one type and are closely arranged in anastomosing strands and cords so that the intervening capillaries come into direct contact with all the cells. The cell nuclei are large and round and the cytoplasm very abundant with a somewhat granular structure. The perfectly clear cells and the eosinophile cells seen in the human parathyroid are not to be found here. Nor are they evident in the parathyroids of various other animals such as the dog, the horse, cow, cat, etc.; occasional cells suggesting the eosinophile type may be seen but in such definite grouping as occurs in the human parathyroid they are not to be found. The structure of the goats parathyroid is shown in the accompanying figure.

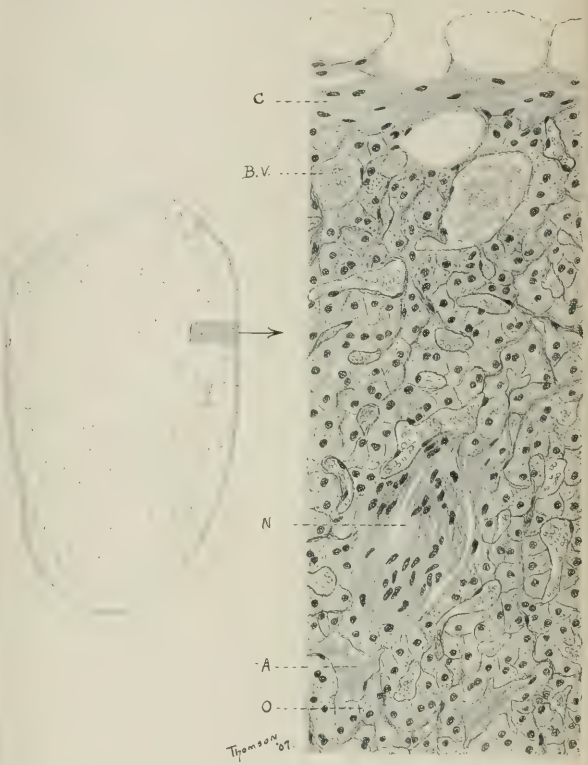
The experiments which we undertook for the purpose of controlling the current statement about tetany in herbivora were carried out on eight goats and five sheep. The two parathyroids embedded in the thymus were removed, sometimes together with part of the thymus and the two thyroid lobes were removed at the same time. Wound healing was perfect in every case.

The histories of these cases are briefly as follows:

Goat A.—Operation on Dec. 13. On Dec. 15 distinct and quite intense twitching was observed in fore and hind legs. At certain moments this was so intense that the goat had not the use of his hind legs which were stretched out stiffly behind. Respiration was not affected and later in the day the twitching practically disappeared. On Dec. 17, the animal was unable to stand, respiration labored, but no tetany. This condition continued until Dec. 19, when he was found dead. At the autopsy no parathyroid tissue was found and no changes in the organs were discoverable which could account for death.

Goat B.—Old goat. Operation June 8, 1907. Thyroid removed with two bodies which subsequently proved to be lymphglands. No symptoms up to Jan. 11, when a second operation was performed, and the two parathyroids removed from the thymus. No symptoms until Jan. 21, when there was definite twitching in the legs and body wall. This disappeared next day and remained absent. There were no symptoms throughout February, but on March 9, the animal was found dead. At the autopsy nothing was found to account for death, and no further parathyroid tissue could be discovered.

Goat C.—Small kid. Operation March 29. Four parathyroids together with thyroid and thymus removed. Animal died of pneumonia March 31, having shown only indefinite quiverings.



Parathyroid of goat. *C*, capsule; *Bv*, blood vessel; *N*, nerve; *A*, alveolus with granular content; *O*, epithelial cells.

Goat D.—Small kid. Operation May 4, 1907. Two parathyroids and both thyroid lobes removed. Accidentally killed May 13, without having shown any symptoms. At autopsy no trace of thyroid or parathyroid tissue.

Goat E.—Small kid. Operation May 5, 1907. Parathyroids, thymus, and thyroid extirpated. No symptoms until May 16, when the animal was found in violent tetany, lying on the floor in convulsions with rapid labored breathing. This passed off later, but distinct twitchings could be felt in the muscles, especially about the head and ears. Next day the same violent tetany reappeared, and the goat died in this attack. At autopsy no trace of parathyroid tissue could be found, nor any lesions in the other organs which could account for death.

Goat F.—Angora kid. Operation May 22. Parathyroids, thymus, and thyroid removed. In this goat which is still alive (July 7) slight twitchings have been observed from time to time, but there has never been any violent tetany. Given several large doses of Liebig's extract without any effect.

Goat G.—Angora kid. Operation May 23. Two parathyroids, thymus, and thyroid removed. Some twitching observed during next three days. Given large doses of Liebig's extract without any effect. May 31, at 6 p. m., the goat was found in violent tetany, legs very stiff, breathing deep and slow, head constantly thrown far back. Next morning it was again found in violent tetanic convulsions, unable to stand, twitchings exactly as in dogs without such great rigidity; fibrillary tremor of tongue well marked. The animal was given subcutaneous injections of ox parathyroid, but the tetany continued together with the opisthotonic drawing back of the head. Later in the evening the weakness and opisthotonos were alone evident, the twitching had stopped. June 2, 10 a. m., again in marked tetany with much rigidity of legs. Found dead at 3 p. m. At autopsy there was found a quite extensive lobular pneumonia.

Goat H.—White kid. Operation May 26. Parathyroids and thyroid lobes from each side extirpated. This animal is still alive July 7, and has shown no symptoms whatever.

The results obtained by operating on sheep were as follows:

Sheep A.—Operation Jan. 8. Two parathyroids and thyroid removed. Only most indefinite twitching observed during next few days. Death occurred Jan. 15 from pneumonia.

Sheep B.—Operation Jan. 8. Two parathyroids and thyroid extirpated. No symptoms up to Feb. 19, when another operation was performed and all the thymus removed from the neck. Death during night.

Sheep C.—Operation March 12. Two parathyroids and thyroid removed. Examination of the thyroid revealed as usual two parathyroids. No symptoms at any time.

Sheep D.—Operation Mar. 14. Two parathyroids, thyroid with two parathyroids and part of thymus removed. No symptoms except slight twitching on Mar. 20. Death from pneumonia Mar. 22.

Sheep E.—Operation Feb. 20, 1907. Parathyroids and thyroid removed. No symptoms up to Mar. 19, when another attempt was made to remove what was left of the thymus in the hope of extirpating any possible accessory parathyroids. No symptoms followed this. Sheep died April 12, much emaciated. No pneumonia.

From these experiments it is seen that there is indeed a very marked difference between the results obtained by parathyroidectomy in the dog and those in such animals as the sheep and goat. Practically no effect whatever was produced in these five sheep, although in at least three of them ample time elapsed for the development of symptoms. It is true that there was observed from time to time a slight twitching, but this was so indefinite that it cannot be regarded as typical tetany. In sheep B, C, and E a marked emaciation followed with some apathy which resembled that occasionally produced in dogs after such an operation but on the whole the results must be regarded as practically negative. All of these sheep were mature animals and as will be seen from the experiments on the goats the most definite results were there obtained in very young ones; possibly further experiments with lambs might show that it is possible to produce tetany in them.

In the case of the goats there was fairly definite twitching without actual tetanic convulsions in four; two showed no symptoms at any time, while two developed perfectly typical and extremely violent tetany leading at least in one case to the death of the animal. The feeding of proteid and extractive material such as Liebig's extract seemed to have no influence whatever upon the outcome of the experiment. From these two positive results, however, it is clear that the extirpation of the parathyroids is not such a completely indifferent proceeding as has generally been stated.

We do not know how to explain satisfactorily the negative results in so many of these animals unless it be that in spite of our extremely careful and conscientious search there are still other masses of parathyroid tissue hidden away somewhere in the neck or thorax. It does not seem reasonable to suppose that organs which are so clearly shown to have a special function in carnivorous and most other animals should be so highly developed in the herbivora and still have no special functional importance.

We may conclude that for some reason, possibly a wide distribution of parathyroid tissue, it is difficult to produce tetany in herbivora by removing the main masses of that tissue but that it is shown to be possible at times by the two cases in which typical violent tetany was produced in the goat.

THE PARATHYROIDS OF THE HORSE.

By WM. L. ESTES, JR.

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The parathyroid gland was discovered in the horse by Sandström, in 1880, who described but one gland situated at the superior extremity of the thyroid body. Moussu repeated Sandström's observations and found the gland situated in the peri-thyroid tissue along the thyroid branch of the thyro-laryngeal artery which comes off the common carotid artery just at the lower pole of the thyroid and passes toward the larynx, supplying the thyroid by a branch given off at its superior pole. Verdun, on the contrary, finds the parathyroid separated from the thyroid only by its capsule; while Blanc asserts he was never able to find one. Jeandelize, in reviewing the subject from the above observations, concludes there must be a variability in position of the parathyroids in this animal. He further believes in the light of comparative anatomy and of experimental evidence that there is another parathyroid constantly present, either embedded in the thyroid itself or situated somewhere in the peri-thyroid tissue. Comparative anatomy teaches that in all other animals there are four parathyroids, two on each side. The only experimental study is that of Moussu, who removed from a horse first the parathyroids and then the thyroids without producing tetany. Therefore Jeandelize leans to the view that the "unknown"

parathyroid lies somewhere in the peri-thyroid tissue; i. e., the horse has four parathyroids, all external and outside the thyroid gland. More recently Rogers and Ferguson mention in a paper on the anatomy of the parathyroid that they find in the horse, usually along the posterior border of the thyroid, an external parathyroid, which they detect with some difficulty from neighboring thyroid and lymphatic glands; and *an internal gland* situated within and near the middle of the thyroid.

Our study was concerned with the anatomy and topography of these parathyroids of the horse. The external gland was found without difficulty; it varies from the size of a marrow fat pea to that of a hazel nut; it is usually pale yellow-gray, occasionally salmon-pink and on congestion assumes a deep purple-red color. Its consistency is soft but not flabby. It has a peculiar lobulated appearance normally, which is not more prominent with congestion. On cut section the perfectly typical coarsely granular appearance is invariably present and distinct lobules can be easily made out with often a central vessel; this permits of ready differentiation between thyroid, lymph gland, and parathyroid; neither of the former resembling on cross section this characteristic picture.

This gland occurs in a somewhat variable position. Out of 125 glands examined: (1) 42 were found closely adherent to the superior pole of the thyroid. (2) 54 were found in the peri-thyroid areolar tissue, always associated with the thyroid branch of the thyro-laryngeal artery. This breaks up close to the superior pole of the thyroid into numerous ramifications which pierce the thyroid directly or follow its lateral border inferiorly and eventually enter its substance. In this mass of vessels the parathyroids of this class are found and therefore they lie near the superior pole of the thyroid. (3) 28 were found adherent to the lateral margin of the thyroid near its middle; in this case the branching of the thyroid artery was unusually low. (4) 1 parathyroid was found at the inferior extremity of the thyroid, loosely adherent. Thus this parathyroid may be considered to be associated with the branching of the thyroid artery, its position varying with the variations of the artery but in the great majority of instances it is situated on or near the superior pole of the thyroid.

Microscopically, the gland is seen to be surrounded by a thin capsule which sends in fibrous strands as a supporting framework carrying blood vessels. The afferent vessels enter the centre of the gland and branch outward to the boundaries. The capillary net-work is extraordinarily rich, the wide capillaries being separated nowhere by more than two cells. It is of interest to note that Evans has found in the human parathyroid a similar central afferent vessel.

The gland tissue occurs in masses and strands irregularly anastomosing and rarely showing anything resembling an alveolar lumen. These masses are made up of anastomosing cords of cells separated as mentioned by very wide capillaries. The cells vary in appearance assuming forms almost like those seen in the human parathyroid. Three varieties may be distinguished fairly well. Of these the first has a spherical or ovoid nucleus, containing many dark staining chromatin granules and a cytoplasm which is quite clear and takes no stain. The second kind, which is the predominant type of cell, has a similar nucleus but its protoplasm is stained a dull lilac faintly granular like ground glass. These are evidently the analogues of the faintly granular cell of the human parathyroid. The third type occurs but rarely in the specimens we have studied and is by no means so distinct as the other types. These cells are found singly, and but for their similarity to certain typical cells in the human gland, they might be regarded as degenerated cells. They have a dense homogeneous deeply stained spherical nucleus of rather small size, surrounded by a large protoplasmic body which is swollen to almost twice the size of the adjacent cells. In the cytoplasm are fine granules which take a pink stain and give the whole cell a dull red appearance.

Of the 125 glands studied 18 or about 15 per cent were found to have cystic structures adherent or continuous with them similar to those often seen bulging from the parathyroid of the cow. They are usually lobulated as if several cysts were attached at a common origin, rarely they form simple swellings on the surface of the gland. No cysts were found in the parathyroid substance. They contain a pink viscous gelatinous mass, at times quite liquid in consistency and easily evacuated when the cyst wall is cut. Microscopically it is seen that the capsule of the parathyroid runs over the cyst and forms its capsule also. In this capsule one sometimes finds masses of what is apparently thymus tissue, raising the question as to whether the cyst may possibly have originated from the thymus rather than the parathyroid. The lining is of flat squamous epithelium sometimes heaped up in several layers. Much of this is desquamated and appears in the form of large round phagocytic cells floating in the fluid content.

To determine the existence of an internal parathyroid the thyroid was hardened and cut into fine slices with a sharp knife, each slice being examined with a dissecting microscope, and suspicious areas further studied by making frozen sections. Small adenomata are extremely frequent in the horse's thyroid, however, and are confusing; even in well stained sections it is often difficult to be sure that one is dealing with an adenoma and not with a bit of parathyroid tissue, nevertheless the distinction can be surely made. In other cases the thyroids were embedded in celloidin and sectioned serially, every tenth section being examined and stained if necessary. Twenty-five glands were thus examined and the parathyroid found in thirteen of them. They seem to be distributed irregularly in the thyroid tissue, occurring often near the superior pole in a rather superficial position, but are sometimes more deeply embedded. Occasionally they are found near the lower pole. The internal parathyroid is pale in color as a rule and may thus be easily confused in gross with any small adenomatous growth though it stands out very sharply from the brown thyroid tissue. In one interesting case two internal parathyroids were found in the same thyroid. They were both darker than the thyroid, and were of comparatively large size; one situated 6 mm. from the superior pole and near

the middle of the gland adjacent to a large artery and the other just beneath the capsule where another large artery pierced it. They were both about 5 mm. in breadth by 4 mm. in length. Their color was found to be due to the overdistension of their capillaries with red blood cells.

The internal parathyroid has the lobular and alveolar structure of the external parathyroid; it is usually separated from the surrounding thyroid tissue by a thin strand of connective tissue but occasionally it shades off so gradually into thyroid that it is hard to tell just where one ends and the other begins; it is exceedingly vascular and invariably adjacent to a blood vessel.

We therefore conclude:

1. The horse has four parathyroids, two on each side.

2. One parathyroid is found at the superior pole of the thyroid in relation to the branching of the thyroid artery.

3. The other parathyroid is found variously placed beneath the capsule of the thyroid, usually near its upper pole.

4. The external gland is much the larger.

5. Further experimental evidence is necessary to prove that parathyroidectomy results in no evil consequences in the horse.

6. The horse resembles the other herbivora in the distribution of its parathyroids.

ON THE PATHOLOGICAL ANATOMY OF LYMPHO-SARCOMA AND ITS STATUS WITH RELATION TO HODGKIN'S DISEASE.

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The confusion which still exists concerning the relationship of various diseased conditions of the hæmopoietic organs to one another, depends, it seems, entirely upon our complete ignorance of their ætiology, for as seen in the case of scrofulous lymph glands, there is no difficulty in defining their status as soon as their cause is known.

No attempt can be made here to discuss all these different conditions, but the material of the Johns Hopkins Hospital has been so rich in two of them, Hodgkin's disease and lympho-sarcoma, that it seems desirable to compare those two especially, since even the anatomical distinctions do not seem clear in all minds as yet, and they are constantly confused.

Such classification as we possess is based entirely upon the morphology and mode of growth and distribution of these lesions, in other words they are distinguished much as a systematic botanist distinguishes and classifies plants. It may perhaps be advantageous to quote Sternberg's attempt at their classification, although since he is one of those who regard Hodgkin's disease as a form of tuberculosis that condition is not included in the classification, but would rationally form number 9 parallel with lympho-sarcoma.

A. Primary diseases of the lymphatic and hæmatopoietic apparatus. Local limited homologous (hyperplastic) tissue growth; (a) With discharge of the cellular elements into the blood and homologous change of the tissue of the lymphatic and hæmopoietic apparatus. (1) Lymphatic apparatus—Lymphocytes in blood. *Lymphatic leukæmia.* (2) Myeloid tissue—myelocytes in blood. *Mixed cell leukæmia.* (b) With slight or no discharge of cellular elements in the blood. (3) Of all lymphatic tissue in diffuse way. *Pseudo-leukæmia.* (4) Of the lymphatic tissue of bone-marrow in form of a tumor. *Lymphatic myeloma.* (5) Of myeloid tissue of bone-marrow in form of a tumor. *Myeloid myeloma.*

B. Atypical growths invading the neighborhood with heterotopic new growths: (a) With discharge of cellular elements in the blood. (6) Of the lymphatic tissue (discharge of ungranulated pathological cells). *Leukosarcomatosis* or *chloro-leukosarcomatosis.* (7) Of myeloid tissue (discharge of granular pathological cells). *Chloro-myelosarkomatosis.* (b) Without discharge of cellular elements into the blood. (8) Of the lymphatic tissue. *Lympho-sarcomatosis.*

The papers of Paltauf and Sternberg in Lubarsch and Ostertag's Ergebnisse, Vols. III_1 and IX_2 form the best summaries of the ideas on these subjects. As to the nature of Hodgkin's disease so much precise description has been written recently that it seems unnecessary to repeat it.[1] Dr. Reed's studies hold good in every detail as far as the histological description and general characters of the growth are concerned, and on studying five additional cases at autopsy we are not inclined to deviate from her ideas that the condition is entirely independent of tuberculosis, and that the new tissue produced has a constant histological character which is easy to distinguish from that seen in any other condition. Briefly described this new tissue consists of a reticulum and connective tissue stroma which becomes denser and more conspicuous with the age of the lesion and in the meshes of which lie at least three types of cells, first the lymphoid cells, sometimes rather elongated, second the large irregular cell with large vesicular nucleus or nuclei, with sharply stained nucleolus and third the eosinophile cells, which last are however inconstant. The picture so constituted is very peculiar and characteristic and may be recognized at any stage although this is more difficult in the late stages when the cells have disappeared in part and the stroma has become very conspic-

[1] Reed, Dorothy M. Johns Hopkins Hospital Reports, Vol. X, p. 133.

Longcope, W. T. Bull. Ayer Clin. Lab. Penn. Hosp., Phila., 1903.

Benda, C. Verhandl. d. deutsch. pathol. Gesellsch. 7 Tagung, 1904.

Sternberg. Ztsch. f. Heilk, 19, 1898.

uous. It was pointed out by Dr. Reed that this new tissue replaces the lymph glands which lose all trace of their original architecture and that nodules of identical tissue may be found in the liver or spleen. She thought that the capsule of the glands was usually respected by the growth so that the glands did not become matted together; nevertheless in the spleen and liver the growth is no respecter of surrounding tissue and since her paper, others have described the invasion and penetration of the capsules of the lymph glands.

The cases which have come under our observation since Dr. Reed's work and which were not described by her were five in number: of these the first three were cases in which involvement of the cervical, axillary, inguinal, retroperitoneal, and other glands were associated with the growth of nodules in the liver and spleen. These exhibited precisely the characters so generally recognized and we had no hesitation in making the diagnosis. The other two cases were however interesting in that in addition to the enlargement of the superficial glands there was extensive invasion of the lungs.

One of these cases was that of a woman aged 32 from whom the enlarged cervical glands were repeatedly extirpated—the examination of these rendered the diagnosis certain. At the autopsy there were found enormously enlarged bronchial glands, with masses of the new tissue extending into each lung and numerous smaller isolated nodules scattered through the lung substance

There were no other organs involved. The sections showed in the pulmonary nodules the characteristic tissue, which had here behaved much as a malignant tumor might behave, filling up some alveoli and compressing others. The trachea was pierced by the tumor growth also and nodules projected into its interior.

The other of the two cases was that of a boy aged 15, in whom there was general enlargement of the lymph glands and flatness over one lung. At autopsy the affected lung was found to be solid and covered by a thick white œdematous pleura. The cut surface showed that most of the lung tissue was replaced by grayish translucent nodules, measuring 1 to 4 mm. in diameter, separated by the opaque yellowish pink compressed lung substance. Microscopically both the glands and the nodules in the lung were found to be composed of a tissue which although very fibrous, could be definitely recognized as the characteristic tissue of Hodgkin's disease.

From several of these cases portions of the tissue have been implanted in the subcutaneous tissues of rabbits, but never has any tuberculosis resulted. Tissue from a recent case from which a gland was extirpated at operation was stained by Levaditi's method and searched minutely for spirochaetæ, but with negative results.

In sharp contrast with these cases, stand eight cases of lympho-sarcoma. As to the definition of the group of lympho-sarcomata or the condition lympho-sarcomatosis we are helped very little by the writers previous to Kundrat, although the condition was seen and recognized as different from leukæmias and forms of sarcoma.

Kundrat describes as lympho-sarcomatosis a more or less widespread lesion with tumor formation arising from a lymph gland, or a group of them or from some lymphoid tissue such as occurs in the intestinal wall, pharynx, etc. Such a tumor mass is composed of a delicate reticulum in the meshes of which lie cells rather larger than lymphoid cells. It fails to respect the capsules of the lymph glands, but grows rapidly and invades and infiltrates the adjacent tissues.

It is thought that the growth may occur by transportation of the cells by way of the lymph stream, as well as by direct extension and implantation, but in these cases too, the continuity of the growth can be fairly well established by discovering the involvement of the intervening lymphatic glands, etc. The tumor tends to spread in loose tissue and in film or plate form over serous surfaces. Metastases in distant organs explainable only by transportation by the blood stream are uncommon.

The tumor forms large infiltrating masses in the mediastinum or in the cervical or pharyngeal region, or in other cases involves the intestinal wall where it may cause a diffuse thickening of the wall with a widening of the intestine at the involved area. In such cases it is not uncommon to find other organs such as the adrenal and pancreas practically buried in an infiltrating mass of such tissue. Where the tumor appears in nodular form in such organs as the heart, kidney, etc., the sharply outlined nodule seen with the naked eye proves to be only a fairly localized infiltration, the muscle fibers or tubules being merely separated by infiltrating cells.

Our eight cases fall perhaps by chance into two fairly distinct groups, in one of which the main lesion consists in a great mediastinal tumor mass with involvement of the thoracic organs without affecting the abdominal organs. In the other group the most striking lesions were in the intestinal wall with other tumor masses involving the other abdominal organs, such as the liver, stomach, pancreas, adrenal, kidneys, etc. These are composed of cells rather larger than those found in the thoracic growths, and contain many large phagocytic cells. It seems probable from this distribution that if it be true that some unknown infectious agent causes this growth, the infection may begin in the one group in the tonsils, pharynx, etc., while in the other cases it invades through the intestinal mucosa.

The cases are as follows:

Case 1.—Autopsy 22, was that of a man aged 27, in whom there was found in addition to great enlargement of the cervical glands, which were matted together, a great mass surrounding the base of the heart and extending downward into the anterior and posterior mediastinum, compressing the lungs. Microscopically the new tissue was found to consist of a delicate stroma containing small lymphoid cells 5-8 in diameter.

Case 2.—Autopsy 1402, that of a colored woman aged 60, in whom at autopsy there was a mass 6 x 8 cms. which lay in front of the root of the aorta, with a similar mass behind; all the pericardial lymph glands were enlarged and the pericardial cavity obliterated by adhesions, and on opening the heart it was found that the tumor mass had grown down over the surface of the heart and had penetrated its muscle so as to partly replace the wall of the right ventricle and to hang in polypoid masses into its lumen. The other organs were not involved.

Microscopically the new tissue is uniform everywhere, and composed of cells measuring 5-12 μ supported by the most inconspicuous reticulum. The cells in this case are sometimes rather elongated and coherent, so as to form a denser tissue than usual.

CASE 3.—Autopsy 2111, was that of a boy 7 years of age, in whom all the lymph glands were enlarged and there was found at autopsy a great mass filling the thorax and embedding the heart and compressing the lungs. There was some invasion of the pectoral muscles and of the pleural and pericardial tissues, but no involvement of the abdominal organs. The cut surface of the tumor appeared as a gray, soft, moist, but fairly coherent tissue, which on section was seen to consist of a very sparse and extremely delicate reticulum, in which lay rounded cells measuring from 4-7 . The bone-marrow is composed of a solid mass of cells resembling those of the tumor and so too are the enlarged lymph glands. The capillaries of the liver are filled with the same cells, and enquiry reveals the fact that during life the blood showed 230,500 leucocytes per cmm., chiefly of the lymphocyte type. Evidently then this case, which is otherwise similar to the first two described, differs from them in the leukæmic condition of the blood and will fall on that account into Sternberg's group of leuco-sarcomata.

The other group is perhaps more uniform in its characters.

CASE 4.—Autopsy 92, woman aged 24, in whom there was found at autopsy a large tumor mass involving the jejunum, which is enormously distended, and its walls infiltrated with the tumor, into a cavity in which the jejunum opens; apparently the tumor growth in the walls of the intestine has greatly distended the lumen and has become ulcerated within. The adjacent mesenteric lymph glands were much enlarged. The tumor tissue which infiltrates the whole thickness of the intestine is composed of a very inconspicuous stroma, with round cells averaging 8 μ in diameter. Certain round spaces in the tumor contain large pale phagocytic cells.

CASE 5.—Autopsy 225, man aged 27, showed multiple areas of tumor growth in the intestine, some of which are slightly ulcerated. There were no metastases except nodules in the liver and kidney. Microscopically the tumor tissue is rather coherent, the cells measuring 5-12 μ in diameter. The tumor growths in the liver and kidney have a distinctly infiltrative character, separating the elements of those organs.

CASE 6.—Autopsy 1842, man aged 39, showed three distinct tumor masses in the walls of the ileum, causing much distension. The tumors were deeply ulcerated but still caused great thickening of the intestinal wall. The corresponding mesenteric glands greatly enlarged by similar tumor masses fill the retroperitoneal tissues and the pelvis.

There were also nodules infiltrating the pancreas and right adrenal gland and metastases to the liver, thymus and some intrathoracic glands. The bone-marrow was dense and opaque.

Microscopically the tumor shows the same character as in the previous case, the cells averaging about 8 μ in diameter, while the interspersed large pale phagocytic cells measure about 20 μ. The pancreas and adrenal are densely infiltrated with the same tumor tissue so that their cells are widely separated from one another. It is of interest to note that a very great number of the cells of the bone-marrow, perhaps even the majority, correspond precisely with the cells of the tumor in size and staining characters. They form a very solid sort of tissue there, and among them are moderate numbers of the large pale phagocytic cells. On the whole the tissue does not look like marrow, there being so few of the cells characteristic of that tissue and the whole structure being replaced by the foreign elements. The presence of cancellous bone, however, makes the situation clear.

CASE 7.—Autopsy 2496, a man aged 57, again shows multiple areas of tumor growth in the intestinal mucosa. Patches of the mucosa were so infiltrated that the transverse folds became thick and rigid, sometimes ulcerated. The whole thickness of the intestinal wall at these areas was infiltrated with the tumor. Mesenteric lymph glands were greatly enlarged and as in the preceding case the pancreas and adrenal were spread out into great masses of tissue by the infiltration of the tumor.

The tumor tissue agrees perfectly in character with that of the preceding cases. The cells measure 8-12 μ and show no specific granulations. There are abundant mitoses. The bone-marrow is densely infiltrated with cells which resemble precisely those of the tumor in form and size.

CASE 8.—Autopsy 2543, a boy aged 7 years, of whom the organs were sent into the laboratory. In this case there were again patches throughout the intestine in which the wall of the intestine was infiltrated with the tumor cells to such a degree that the transverse folds of mucosa stood up rigidly and the whole wall was much thickened. The mesenteric glands were greatly enlarged by the same tissue growth, and as in the preceding case the pancreas and adrenals were embedded in an infiltrating mass of the tumor. In this case there were infiltrated areas in the stomach and spleen, but no bone-marrow was preserved.

Microscopically the tumor tissue is entirely similar to that in the other cases, i. e., it is composed of a very delicate inconspicuous stroma, or reticulum supporting enormous numbers of cells with large vesicular nuclei and measuring 8-12 in diameter with large pale phagocytic cells occasionally interspersed.

From an analysis of these cases the following results:

The three cases which show a mediastinal tumor growth extended to the other thoracic tissue as follows:

Pericardium	2 Cases.
Myocardium	1 "
Pleura	2 "
Bronchial glands	2 "
Pectoral muscles	1 "
Cervical lymph glands	2 "
Other lymph glands	1 "
Tonsil	1 "

In no instance was there any metastasis to the spleen, liver, or other abdominal organs. This in itself seems to confirm strongly Kundrat's idea of the regional distribution of these tumors and shows perhaps that they are not quickly spread about by the blood stream. It is curious that in one of these cases (Case 2) soft polypoid masses of the tumor actually hung in the cavity of the heart and still there were no metastases which could be regarded as due to transportation of cells by the blood stream. The extension by lymphatic channels is however apparently easy, and not only do the bronchial and cervical glands become involved, but occasionally even more distant glands. The serous surfaces may be affected by the appearance of nodules or plates in their substance, but in one of our cases (Case 3) the mediastinal mass was such that the pericardium was rendered quite rigid and the heart beat in a circumscribed cavity hollowed out of the tumor.

Histologically these thoracic tumors are seen to be somewhat different from the rest in that they are composed of rather smaller cells. Of course one cannot generalize from so few cases, but in these three cases the cells measured 5 to 8 μ, 5 to 12 μ, and 4 to 7 μ, respectively. There were in none of them the large phagocytic cells so common in the abdominal forms. It is true that Case 2, was peculiar in showing a rather

coherent tumor tissue, but otherwise it resembled the other two cases very closely.

It is surprising to find that a fairly well outlined picture is produced by the second group of cases in which the intestinal lesions form the constant feature and in which they appear to be the oldest lesions.

There are five cases, and these showed in addition to the intestinal growth lesions elsewhere as follows:

Liver	2 Cases.
Stomach	2 "
Pancreas	3 "
Adrenals	3 "
Kidneys	2 "
Mesenteric glands	4 "
Thymus	1 "
Bone-marrow	1 or 2 "
Tonsil	1 "
Testicle	1 "

In three of the cases 4, 7, and 8, the intestinal lesions formed many patches of thickening of the intestinal wall which did not produce narrowing, but rather the reverse. In these cases ulceration was not very advanced and in some of the patches it might be easily overlooked. In these places the thickness of the valvulæ conniventes which stood up stiffly, much swollen by the infiltration of cells was striking. Such prominent portions of the mucosa soon become ulcerated. In the other two cases the dilatation of the affected portion of the intestine was enormous, so that the gut appeared to open into a great cavity in a mass of the tumor. On careful examination the mode of involvement of the intestinal wall was seen to be similar to that in the other cases, although more extensive. In another case seen at autopsy in Prof. Weichselbaum's laboratory, in Vienna, the intestine throughout considerable lengths was converted into a rigid thick-walled tube. In that case the distribution of the metastases resembled that seen in this series.

In two cases there were single nodules in the liver, while in three both pancreas and adrenals were surrounded and densely infiltrated with the tumor substance. It seems probable that this affection of the pancreas and adrenals was due to extension of the tumors from adjacent affected lymph glands, but we must suppose that the cells reached the liver by the blood stream. This is true too in the two cases in which the kidneys were infiltrated, and in one with a similar affection of the testicle, and probably the involvement of the thymus in one case must also be regarded as hæmatogenous. In two cases the mucosa of the stomach was thickened by the accumulation of cells in much the same way as the intestinal mucosa.

It is generally stated that the bone-marrow is not affected, but in two of three of these cases, in which the bone-marrow was examined it was found to be markedly altered and largely occupied by cells which closely resemble those of the tumor. In the remaining three cases from the group of intestinal tumors, no bone-marrow was saved.

Histologically the members of this group agree very closely with one another. Their cells are rather larger than those of the thoracic tumors; they measured:

6-14 μ
5-12 "
6-10 " or an average of 6.6-12 μ.
8-12 "
8-12 "

There are also large phagocytic cells among the other cells in these cases, although they are not found in the three cases of thoracic tumors. It is seen from this description that there is no especial difficulty in distinguishing between the tissue from a case of Hodgkin's disease and that from a case of lympho-sarcoma; the histological characters are quite constant and quite unlike.

On the other hand although the distribution of the lesions is almost as characteristic and useful in distinguishing the two, one can imagine cases in which it might be impossible to decide definitely without the histological examination of the tissue.

It is more difficult, indeed almost impossible to distinguish the new tissue of a case of lympho-sarcoma from that in the nodular areas of infiltration or in the greatly enlarged lymph glands in leukæmia. Evidently the line to be drawn between these conditions is not a very definite one, for there are cases in which a lympho-sarcoma without leukæmic changes subsequently developed them and in Case 3, of our series there was a distinct, indeed a very great increase in the number of lymphoid cells in the blood with corresponding changes in the bone-marrow. Hence this case is probably wrongly included in the group of lympho-sarcomata according to the morphological subdivision and should properly be classed as a case of leuco-sarcoma supporting in that way Sternberg's classification.

Again there are of course many cases of leukæmia long recognized as such by the blood changes, in which there develop toward the end of life such enormous packets of enlarged glands with masses of lymphoid tissue in the liver, spleen, and other organs, that it is difficult to resist the idea that here we have to do with an infiltrating process somewhat like that in lympho-sarcoma. Even in the acute cases of leukæmia such lymphomatous nodules or areas of infiltration are found in the liver and kidney, but the destructive processes which characterise the lympho-sarcoma are absent here, the bone-marrow changes are prominent as well as those of the blood and thus the morphological distinction is made.

A subdivision of the cases of fairly typical lympho-sarcoma into two groups has been made, but it is of course not to be claimed that all cases of lympho-sarcoma will fall clearly into one or other of these groups. It is probably to a certain extent an accident that ours do so, for it is easy to see from a review of the rather confused literature, that there are many cases in which different distribution of the lesions is recorded and doubtless as stated by Kundrat any region of lymphoid tissue may be the starting point for such growths. The character of the growth and its mode of distribution is however distinctive enough, and so is its histological structure.

In contrast with this a case may be recorded in which it is somewhat difficult to settle the diagnosis in this regard.

E. E. H., man aged about 50 years. Blood count normal, great enlargement of spleen and lymph glands. At autopsy all the lymph glands, and especially those in the retroperitoneal and pelvic regions, were greatly enlarged and occupied by a dense white opaque tissue which did not completely replace the gland, but sometimes left portions of it unaltered. These nodules invaded the adjacent muscles and vertebræ and nodules appeared in the pleura, pericardium, lungs, bronchial walls, etc. The bone-marrow showed microscopically only the response to a general anæmia. The spleen enlarged and hyperæmic, showed no tumor nodules.

Microscopically the tumor consists of one type of cells, lying in a stroma. They are elongated or round or polyhedral and average 9 to 10 μ in diameter. The protoplasm of the cells is so irregular in form as to give the impression that they are coherent in a sort of tissue and not loosely arranged as in the lympho-sarcoma. The tumor everywhere has a highly invasive character. In this case there were no leukæmic changes and the bone-marrow shows only anæmic changes. Nearly all the lymph glands are however enlarged by the presence of a growth which extends through their capsules and mats them together, invading beyond into the muscles, bone and subserous tissues, but scarcely involving the organs. In this we have a sharply differentiated growth easy to outline in the involved lymph glands against the lymphoid structures, formed of coherent tissue, composed of polygonal cells and destroying instead of infiltrating the tissue into which it advances. It seems therefore that this has rather the character of a true sarcoma primary in the lymph glands than that of a lympho-sarcoma.

Such a sarcoma may in some cases resemble even in its distribution the growths which we recognize as lympho-sarcomata, but may be distinguished by their histological characters. Thus in one case there was found at autopsy a large mediastinal tumor growing almost precisely as in Case 3, and metastasising to the thoracic lymph glands, but microscopical study revealed the histological structure of an alveolar sarcoma.

The distinction which may be drawn between the true round celled sarcoma and the lympho-sarcoma depends not so much upon the histological characters of any isolated portion of the tumor as upon the determination of the point of departure of the growth, the manner of growth and the manner of distribution.

In contrast with what has been written in describing the lympho-sarcoma we find the true round cell sarcoma arising not especially from lymphoid tissue, but from the connective tissue at any point, commonly from inter-muscular tissues, periosteal or subcutaneous tissues, etc., where it forms a mass which grows expansively not from multiple or wide spread areas or origin but in one nodule which infiltrates and destroys tissue in its advance. It is much less a characteristic of the true sarcoma than of the lympho-sarcoma, to merely separate the elements of an invaded tissue without bringing about their destruction and it is therefore less common to find even remnants of the invaded tissue buried deep in the tissue of the sarcoma. The mode of growth is thus fairly distinctive in these two conditions. Metastasis takes place in true sarcomata, not so much by mere extension as by the rapid invasion of blood vessels and the production of distant nodules, strictly according to the mechanical principles of the circulation. The involvement of even the draining lymph glands is sometimes lacking, but in other cases the glands are extensively affected. These are things which help to distinguish one form from the other, rather better than the character of the cells and supporting tissue which may show great similarity in the two.

On the whole it seems possible in this anatomical way to outline clearly enough the group of lympho-sarcomata; it is only necessary however that this somewhat artificial classification be borne with patiently until the ætiological factors become known, for then we shall see clearly.

ON THE ANATOMY OF A MYXŒDEMATOUS IDIOT.

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and
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The detailed studies of the anatomical changes resulting from the loss of thyroid function are not yet so numerous that this report will be superfluous.

The case is that of an idiot girl about 13 years of age, who for some time had been an inmate of Bay View Asylum. The history as obtained with difficulty from the Polish mother is as follows:

Ophelia P., 13 years of age. Female, white, Polish. Born of healthy parents. While mother was four months pregnant, a person died in the house. She was in constant terror till Ophelia was born, and thinks this is the cause of her child's trouble. Two other children were born later, normal, but died young. Ophelia nursed the breast and would eat articles of food put in her hands, but could not handle a teaspoon. Said "Papa" and "Mama," and seemed to recognize them, but no one else. Never walked. Mother noticed child's hair was always coarse and that she remained small. Case seen by Dr. Kirk December 13, 1904, and diagnosis of Cretinoid Idiocy made. Family was to be broken up for financial reasons, and patient put in Bay View Asylum.

Mother states child became more and more swollen. Indefinite history of thyroid treatment on entrance to Bay View Asylum. Three days before death the doctor was summoned as the child seemed to be choking up. Given thyroid gr. 1. t. i. d. Improved next day and thyroid stopped. Again worse the next day when the patient failed rapidly and died.

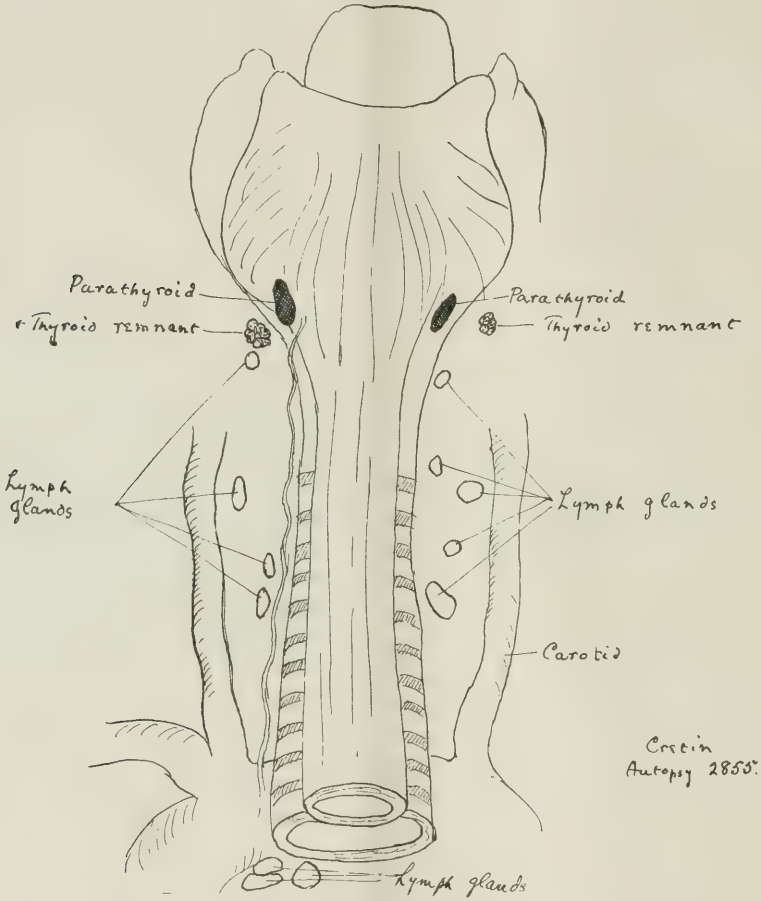

FIG. 1.—Chart of tissues of neck of myxœdematous child.

AUTOPSY No. 2855. February 27, 1907. Dr. Fabyan.

Anatomical diagnosis.—Aplasia of thyroid; cretinism; infantile condition of genitalia, etc.; hypertrophy of hypophysis; aspiration of vomitus; bronchopneumonia; diffuse hæmorrhagic pancreatitis, fat necroses; parenchymatous degeneration of liver and kidneys; focal necroses of liver.

Body is that of an extremely fat white girl, having the appearance of the body of a child six to seven years of age. The hair is cut short, but is rather sparse and coarse, especially on top. The face is expressionless on account of the large amount of adipose tissue. The forehead is prominent. The pupils are equal, measuring 4 mm. in diameter. There are no marked pads of fat beneath the eyes. The lower part of the face is puffy. The teeth are of the adult type for the most part, but are misshapen and irregular.

The supra clavicular pads are well marked. There is no sign of hair in the axillæ or about the pubes. The abdomen is very prominent and the veins stand out over the whole chest. The external genitals are small, but well formed. The arms and legs have a swollen appearance, especially on the dorsa of the feet, but nowhere is there pitting on pressure. The nails are in good condition.

On opening the abdominal cavity the fat of the abdominal wall measures 1½ cm. in thickness, and is pale and œdematous. The cavity contains 400 cc. of clear, straw-colored fluid. The intestines are of normal size and appearance, and are normally disposed, except that the sigmoid flexure has a very long mesentery and can be freely moved about. The pelvis is choked with masses of fat, which is also very abundant about the abdominal organs. The uterus is infantile in character, the ovaries apparently normal.

Pleural and pericardial cavities normal.

Heart weighs 125 gms. The pericardial surface is smooth and there is a moderate deposit of fat. The endocardium and valves are delicate and smooth throughout and the cavities of the heart contain only fluid blood. The foramen ovale is closed. The coronary arteries are delicate and the myocardium is of a uniform normal purplish color.

Lungs.—The bronchi contain considerable quantities of granular material evidently vomitus; the smaller ones are full of a bloody, frothy fluid. The glands at the hilum on both sides are enlarged, deep red, and firm. The pleural surfaces are fairly smooth, but show over the posterior part of the lungs dark purplish areas. On section the upper portions of the lungs are moist, grayish pink, and everywhere air containing, while the lower lobes, especially in the posterior portions, show on section circumscribed, slightly elevated, firm, purplish areas, which are no longer air containing.

Spleen weighs 30 gms. and measures 8 x 4½ x 2½ cm. It is of normal consistency and is of a slaty purple color, and presents a delicate capsule. On section the surface is of a uniform purple color, rather moist. The Malpighian bodies are very conspicuous as small circumscribed grayish dots. The trabeculæ are not prominent. The pulp is slightly increased in amount.

Liver weighs 830 gms. and measures 19 x 13 x 6 cm. The capsule is smooth, and the consistency of the organ normal. The lobulations are readily visible and appear swollen and pale. A few opaque areas are visible. The gall bladder contains a small amount of viscid brown bile. Its mucosa and that of the bile duct is normal.

Stomach is distended with a large amount of semi-solid food. The mucosa appears normal, as does that of the duodenum.

Pancreas measures 11 cm. in length and is of about normal consistency. The external surface presents the usual lobulation of whitish yellow color, surrounded by reddish interlobular lines. Numerous small hæmorrhages are present. Other lobules have a deep brown or purple color. There are a few scattered areas of necrosis involving fat and pancreatic tissue, the largest of these in the tail measures 4 mm. The duct contains a little gelatinous material, but opens beside the bile duct at the end of the papilla and is not bile stained.

Kidneys weigh 150 gms. The left kidney measures 8 x 3 x 3½ cm., while the right which resembles it in all respects measures 8½ x 4½ x 3 cm. The capsule strips easily, leaving a smooth surface with prominent stellate veins. The fœtal lobulations are fairly deep. The cortex on section measures 5 mm. in thickness, the striations are normal in appearance.

Adrenals are small with yellowish gray cortex and dark purple firm medulla.

Uterus measures 3½ cm. from fundus to the cervical os, while the fundus measures 2 cm. in breadth and 6 mm. in thickness. The cavity is very small but otherwise normal. The vagina seems normal. The ovaries measure 2½ x 1 cm. and are apparently normal.

Tonsils, œsophagus and *trachea* normal. There are no thyroid lobes to be found, nor is there any isthmus. The trachea is embedded in fat and loose tissue and there are no signs of either inferior or superior thyroid artery on either side. A careful dissection was made from behind and every structure charted; each gland-like body was labelled and examined microscopically with the results recorded in the chart (Fig. 1). There were found two fairly large parathyroids of normal appearance. The source of their blood supply was not very evident, but must have been from some long but very small arterial branch. They lay symmetrically on each side just at the lower limit of the larynx. No scar of any sort occupied the position normally occupied by the thyroid. Just below and outside the parathyroid on each side were found small lobulated cystic structures as charted. That of the left was filled with perfectly colorless fluid. There were several lymphgland-like masses isolated on each side in the fat near the trachea. Search underneath the arch of the aorta reveals some masses of tissue apparently lymphglands.

Aorta is normal and quite elastic.

Brain.—The skull is of normal thickness, the cerebro-spinal fluid in slight excess. The brain externally shows no great abnormality; any irregularity in the convolutions is very slight.

Hypophysis seems slightly enlarged, measures 17 x 10 x 10 mm.

The points of chief interest in the pathological alterations are to be found in the skin, adipose tissue, thyroid, parathyroid, hypophysis, central nervous system, and skeleton. The other organs showed an infantile condition but otherwise nothing especially interesting.

The skin was, as usual, rather thick and dull looking, hairs were scanty and the sweat glands badly developed. Repeated efforts to stain mucin in the subcutaneous tissue were unavailing.

The adipose tissue was extraordinarily abundant, pale yellowish white and forming not only a thick layer under the skin, but loading the omentum and other usual depots. Microscopically the fat is peculiar in occurring in fine droplets in the adipose tissue cells, instead of one large drop filling each cell.

Microscopical study was made of the two small cyst-like bodies which are shown in the chart (Fig. 1) on each side at the level of the cricoid cartilage. These were hardened in Zenker's fluid and studied in serial sections. They were quite alike, except that one, from the left side, contained an extremely small nodule of parathyroid tissue embedded in its central part. They consist as seen in the figure (Fig. 2) of several small cysts lined with flattened or cubical epithelium, and containing a loose granular sort of colloid which only partly fills each and is loaded with desquamated and pigmented cells. At one side of the cysts in each mass there is a little glandular tissue formed into acini which have scarcely any lumen. A portion of this is figured in another drawing (Fig. 3). It seems unquestionable that this is thyroid tissue, although it does not resemble the normal very closely. The supporting framework of each mass is a dense fibrous tissue in which there are occasional very small alveoli, containing colloid and lined by cubical epithelium, but most of the stroma is devoid of epithelial cells and contains only amorphous masses of brown blood pigment. Such are the very scanty remains of the thyroid lobes. There is enough, however, to suggest that the thyroid rudiment was there and from the presence of the pigment it seems clear that more tissue was there at one time but has been destroyed and has helped to furnish the pigment. It is impossible even to guess at the nature of the process. Further search was made for thyroid tissue, and serial sections were carried through all the central part of the hyoid bone, but no trace of such tissue could be found. Serial sections of the tissue in the front of the larynx also failed to reveal any thyroid tissue, but sections through the root of the tongue taken sagitally in the median line from the level of the foramen cæcum back show a considerable nodule of whitish tissue, just below the epithelial covering exactly in the position of the lingual

duct (Fig. 4). This on microscopical examination proves to consist of thyroid tissue much better preserved than that in the neck and showing numerous alveoli containing colloid, some of the alveoli are very irregular in outline, their walls being thrown up into folds so that they assume a rosette form as in the case of compensatory hypertrophy (cf. Halsted's experimental studies of compensatory hypertrophy of the thyroid in dogs). Colloid is present in the larger alveoli but is not very abundant. The epithelial cells are in general cubical, but some of them are increased in size by the enlargement of their nuclei which then take a deep stain. This is obviously actively functioning tissue differing in that respect from the atrophic nodules found in the neck, but there is in all only a nodule about 2 mm. in diameter, so small that it would have been overlooked had it not been especially searched for. The thyroid insufficiency must have been very nearly complete in this case, and the need so great that even the tiny remnant of differentiable tissue about the rudimentary lingual duct undertook the regeneration as actively as possible. No other trace of thyroid tissue could be found anywhere in the body.

On the other hand the parathyroid glands were well preserved. Aside from the minute nodule found embedded in the left thyroid remnant there was only one on each side, but these were of about normal size and of entirely normal color and consistency, being soft and flabby, and of a reddish-brown color. They lay in the adipose tissue quite free from any adhesions and apparently supplied by small arterial branches possibly from the rudimentary superior thyroid artery.

Microscopically the parathyroid tissue is normal (Fig. 5) except for the fact that it contains no eosinophile cells and that its very wide cell strands seem to be composed of compactly arranged cells with cell protoplasm which is hardly visible, with only faint granules about the margin of the cell to mark out its outline. The arrangement of the tissue is distinctly more compact than is usual in the normal parathyroid and with a low power one seems to be looking at one solid mass of cells. There is no tendency to the formation of alveoli and colloid is almost entirely absent from the gland. In respect to the preservation of the parathyroid without the thyroid, this case resembles those of Maresch and Peucker which are so well known. It seems to offer irrefragable proof of the complete independence of the thyroid and parathyroid glands and the old idea that in case of need the parathyroid which was merely an embryonic rudiment of thyroid tissue could quickly develop into thyroid tissue and replace that which was lost, is in the light of this case as of many others, obviously absurd. The parathyroids after years of thyroid insufficiency show no similarity to thyroid tissue.

The hypophysis was somewhat enlarged, its weight was not taken, but its measurements are, as recorded above, 17 x 10 x 10 mm.

Microscopically the cell masses or alveoli are distinctly larger than normal as may be seen by a comparison of Figs. 6 and 7, which are drawn under the same magnification. The individual cells are greatly enlarged and especially in most areas the chromophobe cells are elongated and radially arranged about a central lumen which often contains a minute quantity of pale staining colloid. The cyanophile cells are very abundant and form a striking feature in the section. There are some eosinophile cells but they are rather shrunken looking and by no means as distinct as in some normal glands. On the whole there is apparently a marked hypertrophy which depends upon the increase not only in the number, but in the size of the cells. The alveolar arrangement is more distinct than in the normal and the colloid production seems to be more abundant. There are some quite large masses of very pale tissue composed almost exclusively of chromophile cells arranged in large swollen looking alveoli with very small central space.

In this respect our case resembles that described by Comte (Zieglers Beiträge, Vol. 23, 1898, p. 90) in that there is an actual hypertrophy of the gland tissue. We incline to agree with him and with Boyce and Beadles as opposed to Schönemann, that the presence of the chromophile cells does not indicate any degenerative process and that the enlargement may perhaps be connected in some way directly or indirectly with the insufficiency of the thyroid. This has been suggested although, as it seems to us, not thoroughly enough studied, in the work of Rogowitsch and Stieda who extirpated the thyroid in rabbits and later studied the changes in the hypophysis which they found hypertrophied. Bayon found in his cases of cretinism an increase in the acidophile cells and in the colloid, and an increase in the density of the stroma, while Schönemann found the hypophysis in his cases of cretinism generally atrophic, although containing all the varieties of cells.

No very complete study of the central nervous system has as yet been made, but this will form the subject of a special note at a later time.

As to the skeleton which we were able to preserve and mount for study the following may be said: There is a general retardation of development and of ossification which may be best observed in the condition of the pelvis, the sternum, the teeth, etc., as well as in the size of the various bones. The skull shows changes especially in the portions forming the face which is very short vertically with prominent jaws and extraordinarily wide nostrils. The teeth are extremely irregular and both sets are represented, those of the first dentition being intercalated between the others, pushed forward or backward and much decayed. Thus of the second dentition in the upper jaw there are four incisors. The canine teeth are not distinctive while the premolars which remain are apparently of the first dentition. One large molar of the second dentition is shown on each side and on each side there is a wisdom tooth beginning to appear; there are in front of the premolar on the right side and in front of the last two molars small decayed teeth distinctly of the first dentition. In the lower jaw there are four incisors of the second dentition with four incisors of the first denti-

FIG. 2.—Thyroid remnant from right side showing cysts, blood pigment, and epithelial remains.

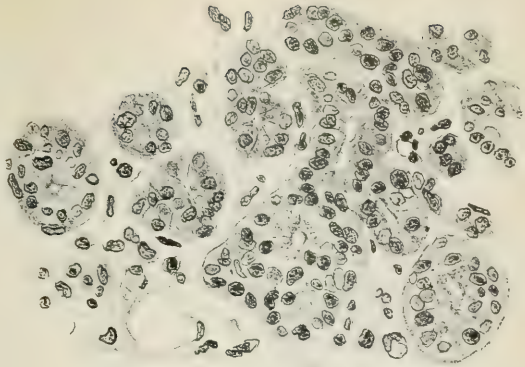

FIG. 3.—Portion of thyroid remnant shown under a lower power in Fig. 2.

FIG. 4.—Thyroid tissue on mid-line at the base of the tongue.

FIG. 5.—Portion of parathyroid from right side.

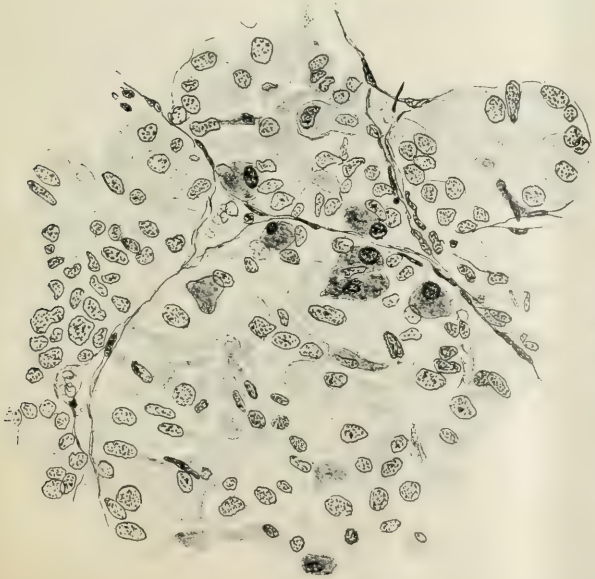

FIG. 6.—Hypophysis showing general hypertrophy.

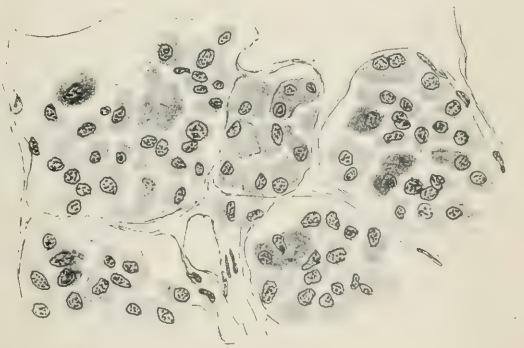

FIG. 7.—From a normal hypophysis drawn under same magnification for comparison.

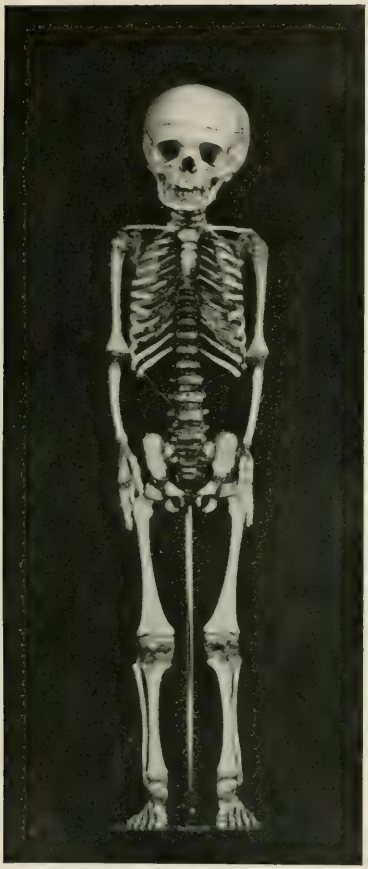

FIG. 8.—Skeleton of myxœdematous child.

FIG. 9.—Skull of myxœdematous child.

tion still persisting but displaced. On the left there is a canine, a premolar and two molars of the second dentition with a tooth of the first dentition between the premolar and the first molar. On the right side a quite similar condition exists and on each side there is a large wisdom tooth just appearing.

The sella turcica is large, measuring 22 mm. transversely, 13 mm. anteroposteriorly and 9 mm. in depth. The spheno occipital union is incomplete and there is a very wide gap between the occipital bone and the petrous portion of the temporal. Wormian bones are very abundant.

The vertebræ seem normal in their conformation as does the whole pectoral arch.

The sternum is composed of five quite separate parts united by cartilage. The arms, legs, and ribs seem well formed, although small. The pelvis is incompletely developed for the age of the child. Normally in the 7th or 8th year the rami of the ischium and pubis become completely united by bone. In the acetabulum the three parts are still separated by a Y shaped strip of cartilage which is continuous with that lining the cavity. This cartilage begins to be ossified from several centres at about the 12th year and the union is completed from the 18th to the 20th year. In this case the rami of the ischium and pubis are still separated by 1 cm. or more and the three portions forming the acetabulum are still quite widely separated.

Measurements of this skeleton may be tabulated as follows with comparisons with the normal measurements as set down by Vierordt and Pfitzner:

Normal Child. 13 years.		Cretin. 13 years.
Height 135-143	cm.	96 cm.
Sitting height 71.3	cm.	56 cm.
Body weight 32-35	kg.	
Pfitzner.		
Length of arm 60	cm.	36 cm.
Length of leg 64	cm.	42 cm.
Length of head 17.4	cm.	15.5 cm.
Breadth of head 14.4	cm.	14 cm.
Height of head 11.5	cm.	12.3 cm.
Circumference of head.. 50.9	cm.	47.5 cm.
Breadth of face..... 11.7	cm.	10.5 cm.
Height of face..... 9.7	cm.	8.5 cm.

Further measurements in this case are as follows:
Nostrils, 24 mm. wide. 20 mm. high.
Nasal bones, 15 mm. long.
Inner canthus to inner canthus, 22 mm.
Between outer angles of orbits, 9.2 cm.
Lower jaw, 9 cm. long, 6½ cm. transversely.
Width of thorax, 15.5 cm.
Length of thorax, 18 cm.
Sternum to tip of ensiform, 10 cm.
Humerus, 15 cm.
Ulna, 11½ cm.
Radius, 10½ cm.
Femur, 21½ cm. (Trochanter—external condyle, 18 cm.)
Fibula, 16½ cm.
Pelvis-sacral promontory to symphysis, 5½ cm.
Transverse diameter, 6½ cm.
Between crests of ilia, 12½ cm.

Langhans has pointed out that the skeletal changes in the cretin are not to be confused with those seen in the new born in cases of chondro dystrophia and further that early synostosis as a cause of retardation of development does not occur. Instead he finds an abnormal persistence of the epiphyseal cartilage and a retardation in the ossification along the epiphyseal lines. This as is seen from the above description is true to a certain extent in our case. We did not saw through the bones because of our wish to preserve the complete skeleton, but it may be seen that while the epiphyses of the humeri are fairly well ossified, those of the femur, tibia and fibula about the knee are very widely separated from the diaphyses. About the elbows and at the head of the femur this retardation is less marked.

The bones are all slender and delicate and in practically all dimensions the cretinoid skeleton is smaller than the normal, while the proportions are fairly well preserved. From this case one would be led to believe that the retardation in growth is due rather to a general disturbance of nutrition than to a special interference with one or other process of bone formation.

LEIOMYOMATA OF THE GASTRO-INTESTINAL TRACT, ASSOCIATED WITH FIBROMATA MOLLUSCA, AND SUBCUTANEOUS HEMANGIOMATA.

By Marshal Fabyan, M. D.,
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These lesions occurred in a white woman, 67 years of age. The clinical history and physical examination were unfortunately very meagre owing to the patient's sensitiveness of her appearance. She first noticed the lumps on her body when she was a little girl but had always refused to have any doctor examine her. Her husband became an invalid, and she supported him for over eighteen years by hard physical work. For eight of these years she was employed in a hospital. One daughter was born but died in childhood. The woman had always been well and never suffered from any chronic gastric symptoms. Three years before death she was removed to the almshouse, having become too weak and infirm to support herself.

At autopsy the body was found to be that of a sparely

built, old white woman, somewhat emaciated. One was immediately struck by the large number of nodular growths scattered over the whole body but especially marked over the anterior surface of the trunk. (See photograph.) A few were present on the scalp and about the ears, forehead, eyelids and mouth, the neck being especially involved. None were noticed on any of the mucous membranes. Over the extremities there were fewer nodules and the forearms and lower legs were comparatively free. The palms and soles were unaffected. The position of the nodules bore no particular relation to the course of the nerves. Their size varied from a few millimetres to 3-4 cm. in diameter, the larger ones being situated on the thighs. They were usually round or oval and quite circumscribed, but occasionally one or more coalesced, giving a lobulated appearance. Some protruded but slightly above the surface; others were elevated on a broad base and still others were supported on a short pedicle. In the main their character was sessile. Over the sacral region many of the nodules had begun to slough owing to pressure.

The skin over many of the larger was white, soft, and usually wrinkled as if a certain amount of absorption had taken place, but over the smaller, was distinctly adherent to the underlying structures. All the nodules had a uniform, moderately firm consistency and elasticity. No areas of pigmentation were observed.

On dissection of the skin the smaller nodules were adherent to the corium; others lay at the margin of the corium and subcutis, as flattened oval masses, about 1 cm. in diameter, causing no bulging of the epidermis. The larger nodules were more or less definitely circumscribed and could be readily separated from the corium and subcutis. Occasionally, they were thick enough to pass completely through the subcutis and lay on the muscle. These growths also assumed a flattened, rounded shape, extending finger-like projections into the subcutis but in some instances protruded through the corium becoming intimately adherent to it. One or two minute purplish red tumors were found in the subcutaneous tissue.

On section the nodules were smooth, firm, glistening, and translucent or slightly opaque. The larger had a distinct œdematous appearance but no fluid could be expressed. No internal structure could be made out. Those deeply situated were quite vascular.

No nodular thickenings of the larger nerve trunks or of the cutaneous nerves were noticed.

The other lesions of interest were found in the gastro-intestinal tract. The stomach was somewhat dilated and showed considerable post-mortem self-digestion. Scattered over the posterior wall in the fundus region, in an area 10-12 cm., were a dozen or more fine nodular thickenings more or less elongated, their axes being parallel to the long axis of the stomach. They bulged the peritoneal surface slightly. On section they were of a grayish white color, firm and definitely circumscribed in a few instances. The largest one measured 4 x 3 mm. The mucous surface so far as one could judge after post-mortem changes gave no evidence of their presence.

In the upper portion of the ileum a subserous nodule 15 x 13 mm. was encountered, sessile in character. The mucous membrane at its point of attachment was somewhat puckered and presented 2-3 pin-point whitish elevations beneath the intact surface. The nodule was firm and elastic, and presented on section a pinkish smooth surface composed of bundles of fibres cut in different planes.

There were no uterine myomata.

The anatomical lesions present other than those described were as follows: Arteriosclerosis; chronic fibrous myocarditis; brown atrophy of the heart muscle; chronic nephritis; emphysema; tubercular apical scar; chronic bronchitis; chronic fibrous pleuritis; anthracosis; chronic tubercular lymph-adenitis (bronchial); chronic tubercles in liver; scoliosis.

Microscopically, the skin nodules were composed of masses of delicate, wavy connective tissue lying, just beneath the epidermis which had a more or less stretched appearance, the papillæ being few in number and flattened, or in the lower corium. The nodules rarely lay side by side, separated by a few strands of normal connective tissue, or one beneath the other. No definite capsule was present and although the margin of a tumor was more or less irregular, there was no distinct infiltration. A few small outlying areas proved to be separate nodules. Sweat glands, hair follicles, smooth muscle, and fat tissue were included in the growths and showed atrophy. Involvement of the sweat glands, in those superficially situated, was most often noted appearing conspicuously in the microscopical nodules.

In many of the growths, especially the larger ones, the external portion was composed of connective-tissue fibres running in a circular direction with long parallel mature nuclei and deep eosin staining cytoplasm. More internally were nuclei of the immature type, being of irregular shapes, less elongated, more oval and vesicular. These lay in an œdematous meshwork of delicate wavy fibrils which stained lightly with eosin and the connective-tissue stains (Mallory, Van Gieson). The degree of cellularity and fibrosis varied in different parts of a nodule. A few mast cells and lymphocytes were present, the latter occasionally occurring in small groups. No elastic or myxomatous tissue could be demonstrated by special stains. Blood vessels were quite numerous and larger than those ordinarly seen in the corium. The cells forming them were usually easily differentiated from the tumor cells, having nuclei uniformly large, oval and more vesicular but in some instances blended with the surrounding tissue so closely as to make the individual cell indistinguishable from a tumor cell. The nerve tissue in these nodules varied from practically none to a moderate amount.

No abnormality was noted in its structure save a rather prominent perineurium which took a much deeper red with Van Gieson's stain than the surrounding connective tissue. No microscopical lesion of the cutaneous nerves or of the larger nerve trunks was found.

A few small minute tumors lying in the subcutis were very cellular, the nuclei being large, oval, vesicular, and occasionally showing mitotic figures. The blood vessels in these were very profuse and dilated in one or two instances.

The purplish-red tumors were small hemangiomata.

The same uniformity of appearance was present in the gastric nodules as in the skin fibromata. In every instance a definite myoma was present, lying always in the outer coat of the muscularis, which gave no evidence of hypertrophy. Although in no case was a capsule present the myomatous tissue was sharply differentiated from the normal muscularis. The fibres of the latter passed on either side of the tumor and were occasionally ruptured on the peritoneal side. Each nodule was more or less elongated and composed of bundles of smooth muscle fibres arranged in irregular whorls; typical nuclei were frequently closely packed together. The intervening tissue had a homogeneous strand-like appearance and practically did not stain with eosin although markedly with Van Gieson.

The amount of this degenerated tissue varied from a minimum in microscopical nodules to an almost complete obliteration of the cellular element in some of the larger ones. The nuclei in the latter case were usually collected about the periphery. The blood supply was practically nil. In general these myomata resembled closely the ordinary uterine myoma.

The subserous intestinal nodule proved to be a myoma containing areas in which the fibrous tissue predominated. At its point of attachment to the intestinal wall the external layer of the muscularis was interrupted, the ends passing directly into the tumor for some distance, staining well with eosin. Bundles of smooth muscle cells were bound together by a small amount of connective tissue easily demonstrated by special stains. About the periphery these cells had a circular course, and a thin, fibrous capsule was present. Throughout the nodules generally were many oval and elongated homogeneous areas running parallel to the muscle fibres, and occasionally vacuolated. The muscle nuclei crossed these areas or were continuous with them, suggesting the explanation that they were due to hyaline degeneration of the muscle. The blood supply was abundant within the nodule and the vessels in the adjacent submucosa were very large and conspicuous.

In brief we have in a woman past middle life numerous fibromata of the skin associated with myomata of the gastro-intestinal tract. The other lesions present were those compatible with a person of her age.

Multiple primary tumors in one individual are not uncommon and as many as five in one instance have been reported (Ribbert). In some cases these may spring from associated tissues and may be said to bear some relation to each other but frequently different tissues are involved and there appears then to be no definite ætiology beyond a certain predisposition.

Much has been written concerning the origin of the skin fibromata. Rokitansky believed that they sprang from the deep intercellular spaces of the corium; others considered the connective tissue about the hair follicles and sebaceous glands the primary seat, while Virchow favored the connective tissue of the fat tissue as the starting point. Von Recklinghausen's observations have gone far to prove the growth to be in reality a neuro-fibroma in many instances and his work has been confirmed by Unna. The subcutaneous nodules are seen to have a more or less plexiform arrangement and the nerve tissue may be almost or entirely replaced by connective tissue. The general characteristics of these neuro-fibromata tally fairly well with the above description but there is usually involvement of the cutaneous nerves as well as larger nerve trunks which was not present in this case. In some instances where both the conditions were present the case was reported as one of fibromata molluscum associated with neuro-fibromata. In fact there is a good deal of confusion of terms and Crocker in his text-book mentions fibroma molluscum and neuro-fibroma as synonymous for fibroma of the skin. Unna considers that there is a widely distributed myxomatous change in the connective-tissue cells peculiar to neuro-fibromata which is of interest from a differential point of view. No positive results were obtained in this case and in the absence of any nerve involvement one does not seem warranted in making the diagnosis of neuro-fibroma. Ribbert favors Cohnheim's theory of embryonic cell inclusions as the ætiological factor in the condition.

The tumors here described correspond best to the so-called fibroma molluscum, a term first made use of by Bateman. All the general characteristics are illustrated here, but occasionally remnants of elastic tissue have been seen in the tumors.

Taylor has made an interesting report of the development of these nodules. There is first a slight uplifting of the skin which may have a pink color and be soft as if thinned. The prominences become round or oval, their axes tending to follow the line of the ribs on the trunk. Growth may continue slowly or the nodules may remain stationary for long periods. Those of early life are more or less gelatinous but in old age they are dense, firm and less liable to undergo involution. In rapid growth they may become firmly attached to the epidermis but later separate from it.

More advanced types may show tumors of a pendulous character, pigmentation, exotoses and neoplasms of the gums and palate. Vörmer reported a case with marked pigmenta-

tion in which microscopically a pigment fleck showed a minute fibroma molluscum. These patients may suffer from marasmus and psychical disturbances (Mayer) as well as other infirmities. Hebra considers that there is a constitutional predisposition as in many of the patients the condition can be traced to early infancy. In the case I report there was a history of early involvement of the skin, but nothing is known of the patient's family record. There was no pigmentation or mental deficiency. The progressive weakness might be explained by advancing age.

Myomata of the gastro-intestinal tract are by no means common, being very rare in the œsophagus. A myoma of the stomach wall is relatively rare and only a few cases of multiple myomata of the stomach have been reported. They are usually situated about the cardiac orifice and greater curvature (Rokitansky, Fenwick, Kidd) but may lie adjacent to the pylorus and cause symptoms of obstruction (Herford).

Their ordinary size is that of a pea, although enormous tumors have been described. Perls Neelsen reported a case in which a subserous myoma of the stomach reached as low as the pelvis and weighed 6 kilos. In some cases they have been associated with uterine myomata but this was thought to be a coincidence. None were present in this case.

The ætiology of these tumors is again doubtful, although Cohnheim's theory is usually held. The finding of aberrant bits of liver and pancreas associated with these tumors has strengthened this view (Cohn). They spring from the muscularis mucosa and on developing project toward the mucosa or peritoneum, becoming polypoid in character.

The unusual point in this case was the multiplicity of the tumors which were too insignificant to cause any derangement of the gastric functions. Furthermore, they all originated from the outer layer of the muscularis which was not hypertrophied as has sometimes been the case, giving rise to the opinion that these tumors resulted from such an hypertrophy (Ribbert, Steiner, Böttcher). In every instance the general structure resembled that of a uterine myoma; the relative amounts of cellular and fibrous tissue varying with the individual nodule, the former, as a rule, predominating in the smaller ones. In no case was there a blending of the myomatous tissue with the normal muscularis.

The symptoms arising from such tumors other than obstruction described already are chiefly due to ulceration of the mucosa with hæmorrhage which may prove fatal. As a rule, the tumors are small, slow growing and symptomless.

Various regressive changes have been noted in these myomata (Cohn). Fenwick states that the submucous type is prone to cystic degeneration, while sarcomatous changes may appear in the subserous type. Von Eising reports a case of two gastric myomata in which one was of a typical myomatous structure while the other was sarcomatous.

Intestinal myomata are not at all rare and their multiplicity is characteristic of the tumor (Mercer, Steiner). They usually lie in the lumen of the bowel. The one here described conforms to the general descriptions and requires no elaboration. The submucous type when large enough may cause stenosis and intussusception.

The interesting points of the case described are:

(a) The marked involvement of the skin with fibromata mollusca.

(b) The association of this condition with gastro-intestinal myomata.

(c) The multiplicity of the gastric myomata.

(d) The constant involvement of the outer layer of the muscularis in every instance.

(e) The presence of subcutaneous hemangiomata.

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DISSEMINATED SUBCUTANEOUS FAT NECROSIS, OCCURRING IN AN INFANT WITHOUT OTHER LESIONS.

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The case was that of an infant, born at term, of a healthy colored woman, single; 22 years old. There was a history of still birth four years before. The present pregnancy was normal but the mother had a slight puerperal infection and developed mumps two days after delivery. She was discharged well eighteen days after her delivery.

The child, a boy, was somewhat asphyxiated at birth owing to pressure on the cord, but was revived in fifteen minutes. He was well developed, being 46 cm. in length, and weighing 2970 gms. at birth. He suffered the usual initial loss of weight, but fourteen days, later when he died, weighed 3050 gms.

He was breast fed every three hours the first two days until mumps developed in the mother when he received milk ℥i with sodium citrate gr.i every two hours. Three days later the amount of milk was increased to ℥iss. The stools were composed first of meconium, then they became yellow and after being put on artificial feeding were described as white; well digested.

On the third day of life numerous so-called "abscesses' were seen on both cheeks, both forearms and on the back of the head, one buttock, and on the right lower leg. The skin over these swellings was injected. All but the abscess of the right cheek were described as not going on to suppuration and became absorbed. Two drachms of pus were obtained on incision of the swelling of the right cheek, after which healing apparently began. Cultures of the material expressed remained sterile. On the fourteenth day of life the child turned on his face while the nurse was out of the room and was suffocated. An autopsy was performed thirteen hours after death.

The body was that of a well-developed and nourished, colored male infant. The right cheek was very slightly swollen and the skin over an area just anterior to the parotid gland at a level with the upper gum was slightly purplish in color.

A pin-point abrasion was present through which the interne said only a small amount of turbid bloody fluid had been expressed the last few days. The subcutaneous tissue at this point was indurated and on incision a small softened area with a homogeneous opaque, yellowish white periphery was visible. The softened area had the appearance of tallow stained by blood; the periphery, that of typical fat necrosis. The various areas described clinically could be made out as localized areas of induration in the subcutaneous tissue which rarely caused any distinct swelling or discoloration of the skin. A marked symmetry of the lesions on the cheeks and forearms was noted. Other nodules were found on the right arm and leg, all showing a typical picture of fat necrosis. In some the central portion had begun to soften, and could be expressed on slight pressure; it was composed of a greenish yellow material. Cultures from these various areas remained sterile.

Other points noted were as follows: A few subpericardial and subpleural ecchymoses; no macroscopic areas of fat necrosis about the pancreas or throughout the abdominal cavity. The stomach was slightly dilated and contained a white smooth mass 4 x 3 x 3 cms. which had a firm elastic consistency. On section it was found to be laminated and could be torn with difficulty.

Microscopically, the pancreas and areas of fat necrosis are of interest. Many sections of the pancreas failed to show any pathological lesion. In some areas the supporting tissue was slightly œdematous, but in general the islands of Langerhans, acini, and ducts had the appearance of normal histological tissue.

Sections of the right cheek showed an area of 2 x 1½ cm. of typical fat necrosis. The tissue was involved from just beneath the corium externally to the lining membrane of the mouth. (Unfortunately, the parotid gland was not included in the specimen.) The central portion of the space was occupied by a large necrotic area without structure, surrounded by other smaller irregular ones in which the architecture was still preserved. The former contained a granular debris, degenerated fibrin, and red blood cells, including many necrotic polyblastic cells. One area of degenerated fibrin was becoming organized. In the latter smaller areas the general outline of the cells was preserved but stained a diffuse pink, the nuclei failing to stain. Many of the fat spaces had a diffuse pinkish color in which a fine network or delicate lines radiating out from a central point were observed. This radial appearance was doubtless due to spaces left by the dissolved fatty acid crystals. Surrounding these necrotic areas the normal fat tissue septa were large and conspicuous, due to a proliferation of the fixed cells together with an infiltration of wandering cells chiefly of the mononuclear type. This cellular infiltration occurred more or less grouped especially about the larger connective-tissue septa. Large round cells with vesicular nuclei and cytoplasm studded with fat globules (Opie) were also seen. Scattered through this zone were numerous multinucleated cells, the nuclei usually being collected at one pole. Occasionally, necrotic tissue adjoined perfectly normal fat tissue and in some areas the coagulative necrosis had included some of the tissue in which proliferation had taken place.

Sections from the other nodules showed a similar picture of fat necrosis with slight variations. Numerous fine pointed slits without definite arrangement were occasionally present, evidently spaces formally occupied by fatty crystals.

In some sections the outline of the fat necrosis was sharply limited, and in others the process had extended into the subcutis.

In brief we have a case in which multiple areas of fat tissue necrosis occurred in the subcutaneous tissue of a well-nourished but not obese infant, and without any apparent involvement of the pancreas. Had not death supervened by accidental suffocation clinically the prognosis in regard to what were considered multiple subcutaneous abscesses was good. Nothing in the child's condition suggested any serious disease. That the stomach at any future time could have digested the mass of curdled milk seems impossible. The natural course would probably have been a steady increase in its size by further deposits until symptoms referable to the stomach developed.

Fat necrosis has been noted many times at operations and autopsies. It is especially common in and about the pancreas, in the omentum, mesentery, and scattered more or less profusely throughout the abdominal cavity. At times even more distant involvement has been seen in the subpleural and subpericardial fat and even in the subcutaneous tissue (Chiari, Hanseman).

Autopsies on domestic animals, especially the hog, occasionally show areas of spontaneous fat necrosis (Heller, Balser, Williams).

As to the causes of this necrosis various theories have been advanced from that of Balser, who first described the condition in detail and considered it due to an over-production of fat cells, to the generally accepted view that the condition is intimately connected with disease of the pancreas. Its more frequent occurrence in and about the pancreas (5 out of 6 cases reported by Chiari) is striking and there has been much discussion as to whether the various pathological lesions found in the pancreas in these cases were not the result of the fat necrosis or whether both might not be due to some other cause. It now seems well established that disease of the pancreas may give rise to areas of fat necrosis and that given the former in any case, we are justified in assuming it to be the probable cause of the latter. That such an ætiology would also explain the occurrence of distant areas of fat necrosis has been doubted.

Various bacteria have been isolated from time to time and considered the cause of fat necrosis. Cocci and bacilli have been obtained by culture and usually identified as belonging to the commoner pyogenic or intestinal types (Ponfick). Although bacteria may undoubtedly play a part (Flexner) they probably act secondarily, the necrotic tissue predisposing to their invasion (Fraenkel).

As soon as it was suggested that certain lesions of the pancreas might cause fat necrosis numerous experiments were performed, and by injury typical areas of fat necrosis were obtained, not only in and about the pancreas and abdominal cavity, but even in the subcutaneous fat about the pubes in those animals which lived several weeks after the operation (Opie). The absence of any infection in these cases proved that the lesions may be produced independently of bacteria. Any diverting of the pancreatic juice from its normal course was usually followed by lesions in the adjoining or distant fat tissue and in all these instances the fat splitting ferment could be demonstrated (Flexner). The variety of irritants causing an acute pancreatitis on injection into the pancreatic duct was quite remarkable, even bile (Opie) and gastric juice (Flexner and Pearce) proving successful in later experiments. But in the case here described no lesion was apparent in the pancreas and we must look further for a cause.

Fat necrosis has been described as a disease entity, but Opie believes that it is always due to a pancreatic lesion. He considers that fat necrosis bears the same relation to pancreatic disease that jaundice bears to hepatic disease. However, there are cases in literature in which no lesion of the pancreas was noted. (Harrington, Körte.) Hanseman reports a case of subcutaneous fat necrosis in which he was unable to find any lesion of the pancreas except what might be considered due to post-mortem change. Flexner and Fraenkel report cases of disseminated fat necrosis without lesions of the pancreas. Gall stones were present in these cases. Rolleston considers the necrosis may be the result of a trophic disturbance of the abdominal sympathetic nerves. How this would account for subcutaneous lesions is not clear. Fitz concludes that in those cases in which the pancreas is uninvolved a primary cause may lie in the biliary tract or stomach. Whether a firm, heavy mass, as described in the stomach of this case could have given rise to the lesions seems doubtful when we consider the extensive subcutaneous involvement without internal signs. The process is considered by Chiari comparable to any retrograde metamorphosis; degeneration of the tissue being followed by simple necrosis. He has seen marked lesions of the pancreas without fat necrosis and vice versa and concludes they are not closely related.

Chiari found fat necrosis in an infant one day old with extensive syphilitic changes especially of the pancreas. This is the only other case I have been able to find in which the necrosis occured in very early life. The text-books do not consider the condition at all or speak of the diseases of the pancreas as practically unknown in infancy and childhood, with the exception of the general tissue changes such as occur in syphilis. Rotch states that the pancreatic power of digesting fat seems to be slight in the early months of life.

To sum up: In an apparently well-nourished infant we found typical areas of fat tissue necrosis.

No bacterial ætiology could be demonstrated.

No lesion of the pancreas was found nor were there lesions about the organ to suggest it.

The most advanced lesion in the present case lay in the right cheek in close proximity to the parotid gland.

Considering the fact that the parotid glands resemble the pancreas rather remarkably in structure and function, developing at about the same period of fœtal life, and that the mother developed mumps two days after the birth of the child, is it not possible that the gland posseses at this early period a lipolytic ferment which disappears in later life and

that an inflamation of the gland was the cause of the fat necrosis in this instance? The period for such extensive involvement was very brief according to evidence derived from experiments on the pancreas.

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A CASE OF PRIMARY CARCINOMA SUPERVENING IN A CIRRHOTIC LIVER.

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The lesions occurred in a colored man 62 years old. He was quite weak when first seen and could state nothing of importance in either his family or personal history. He remembered only that he had been sick a long time; his chief complaints being weakness and a swollen abdomen. Physical examination revealed a much emaciated man in whom arterio-sclerosis was marked. The thorax except for very superficial breathing and a systolic murmur over the heart's apex was negative. The abdomen was tympanitic and presented in the right upper quadrant just below the costal margin an irregular nodular prominence, evidently the liver. The liver edge was made out 5 inches below the right costal margin in the mammillary line; hepatic dullness beginning above the sixth rib. The spleen was not palpated nor were any enlarged glands made out. The patient grew steadily weaker and died one month after the first observation.

At autopsy, the body was that of a much emaciated colored man. One superficial vein on the abdominal wall was prominent but there was no marked abdominal distension. The feet and ankles showed slight pitting on pressure. On incision the abdominal cavity was found to contain about three quarts of straw colored fluid. The intestines were collapsed. The thickened and irregular edge of the liver extended below the costal margin 3 cm. in the right mammillary line and protruding beyond this for a distance of 3 cm. further was a much distended gall bladder which contained brownish viscid bile and one small stone. Marked perihepatitis was present.

A detailed description of the autopsy is not necessary and only the findings in the liver and lungs will be reported in full. The anatomical diagnosis of the other lesions found was as follows: Acute hæmorrhagic pancreatitis; arterio-sclerosis; coronary sclerosis; chronic fibrous myocarditis (calcification of muscle fibres); brown atrophy; chronic passive congestion of the viscera; œsophageal varices; chronic nephritis; chronic splenic tumor; fibroid nodules and old infarct of spleen; perisplenitis.

On lifting the heart, the inferior vena cava appeared much distended as if by a solid mass and incision disclosed a plug extending up and about 3-5 cm. from the diaphragm. It was composed of a mass of fine wavy threads 1-2 mm. in diameter forming a dense twisted tangle with many loose ends extending beyond the limits of the plug.

The liver weighed 1300 gms., and measured 21 x 14 x 7 cm. The anterior surface presented numerous nodules more or less grouped, the size varying from ½ to 3 cm. in diameter. Their color of grayish yellow and white contrasted

with the surrounding liver substance which was of a purplish red hue. A few of the nodules were distinctly green or had a purplish centre. The inferior surface also presented many groups of these grayish white nodules. None showed umbilication. Between the prominences the surface was only slightly irregular and not at all of a hobnailed appearance; the consistency of the organ was, however, distinctly increased. A red thrombus was present in the portal vein extending out of the liver some 3 cm., and into its substance for a slightly greater distance.

On section (Fig. 1) most of the liver substance, especially in the central portion and right lobe was replaced by new growth. Elsewhere the tissue was of a deep purple color, and presented numerous glistening strands of connective tissue. The new growth was arranged in rounded areas a few millimetres to 2 or 3 cm. in diameter, in many instances being distinctly encapsulated. Some were white or yellowish white; others were bile stained, especially in the right lobe and still others were of a bluish-purple color. The smaller nodules had a markedly translucent appearance which persisted in the periphery of the larger tumors. The latter usually had opaque, whitish centres and some had already begun to soften and were composed of a dry granular material.

Many of the vessels were dilated and securely plugged by a cauliflower mass of new growth (Fig. 1). In one or two of the larger vessels this advancing growth presented a blunt, circumscribed end.

Microscopically, the liver presented a thickened capsule, and a diffuse rather marked connective-tissue growth of the intra-lobular type. Associated with this was an infiltration of round cells, chiefly of the mononuclear type, and a proliferation of the bile ducts; the latter quite conspicuous in some areas. The lobules were of normal size or composd of only 3-4 cells. In some areas the capillaries were much distended with blood compressing the liver cells; in others, atrophy of the cells was present without the conspicuous capillaries, the cells being small, deeply pigmented and occasionally fatty and replaced in part by connective tissue. In others there was vacuolation of the protoplasm which stained less well with eosin, while the nucleus took a deeper color. Occupying a small portion of the same lobule or comprising considerable areas were newly formed liver cells, atypically arranged and of a much larger size than the normal cells, staining lightly and more diffusely with eosin. The nuclei were more vesicular.

In this cirrhotic liver, the cells of the new growth were arranged in rounded masses (Fig. 3), the larger ones being bounded by dense strands of intralobular connective tissue. Occasionally, a nodule measured only 12-14 cells in diameter. The periphery of such a small area might be a dense fibrous band; a delicate strand of connective tissue or the tumor cells actually join perfectly normal liver cells or those of the hypertrophied type. Although the general outline was more or less circular and fairly even, it was quite common to see normal liver cells included in tumor tissue and vice versa (Fig. 2). Some nodules were evidently of especially rapid growth and in such instances the surrounding liver cells were compressed into concentric rings, the capillaries collapsing (Fig. 3). The tumor cells were grouped together sometimes in masses, sometimes in the ordinary structure of liver tissue, but of a much coarser type; *i. e.,* the strands were several cells thick or the capillaries between them very conspicuous, almost angiomatous in character. The more usual picture was one between these two extremes. The protoplasmic boundaries of the cells were rarely distinct, and as a rule, only slightly indicated. Their size varied from that of a small liver cell to 4-6 times their size. The protoplasm of the tumor cell stained a darker, slightly purple color, occasionally showing vacuolation. The nucleus varied in size and shape. As a rule, it was slightly larger, two or three times the size of a nucleus of a liver cell, and oval (Fig. 2). The nuclear margin was distinct, the inner surface having a roughened appearance owing to minute dots of chromatin which were also scattered through the central portion, occasionally forming a delicate network. Near the centre, was ordinarily a nucleolus of irregular outline, and not always stained uniformly. The nucleus as a whole had a slight diffuse stain or was colorless save for the chromatin particles. Nuclear figures were present in great numbers and in all varieties of shapes and atypical arrangement (Fig. 4). Cells undergoing nuclear division often lay in a vacuole, and occasionally were very large with lightly staining protoplasm. A few multinucleated cells were present, and some polyblastic cells were observed among the carcinomatous cells and in the fibrous septa.

Other sections showed large areas of new growth which had undergone necrosis. The general structure had been preserved, but the whole area stained a light diffuse pink with eosin, nuclear debris being present about the periphery. Some of these areas had gone on to actual disintegration and polymorphonuclear leucocytes were in evidence.

A few nodular areas which stained lightly were found microscopically to be composed of tumor cells in which the protoplasm had been more or less entirely replaced by fine fat globules. The nuclei still retained their characteristic appearance, and were conspicuous.

Many of the portal vessels were plugged by masses of tumor cells (Fig. 5) covered in every instance by endothelium (Fig. 6). The cells nearest the centre of such a mass were often completely necrotic. No blood vessels could be made out in most of these plugs. The larger vessels contain two or more clumps of tumor cells, each with its endothelial covering.

The mass plugging the inferior vena cava was composed of numerous columns of tumor cells cut in various planes. Each mass had its endothelial covering and in many there were sharply circumscribed central necrotic areas, hyaline in some instances, becoming organized in others.

The lungs in gross were emphysematous and deeply pigmented. Lying free in the right pulmonary artery was a small tangle similar to the worm-like threads seen in the vena cava. Close inspection of the cut surface of either lung

FIG. 1. Photograph. Section of liver. Primary carcinoma.

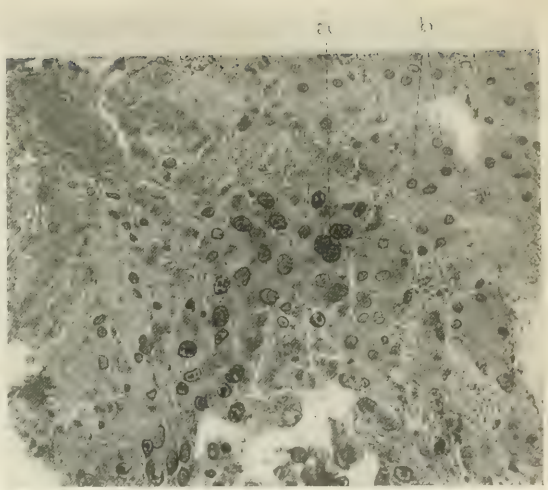

FIG. 2.—Photomicrograph. Tumor cells included between normal liver cells: (*a*) tumor cell nuclei; (*b*) liver cell nuclei.

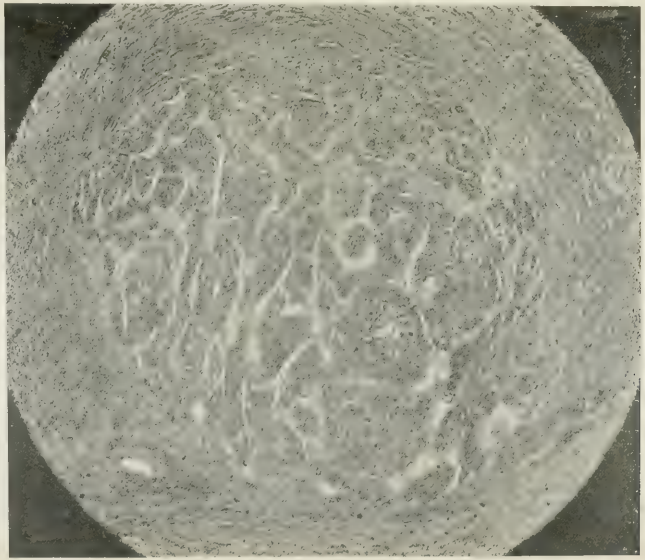

FIG. 3.—Photomicrograph. Active nodule of new growth.

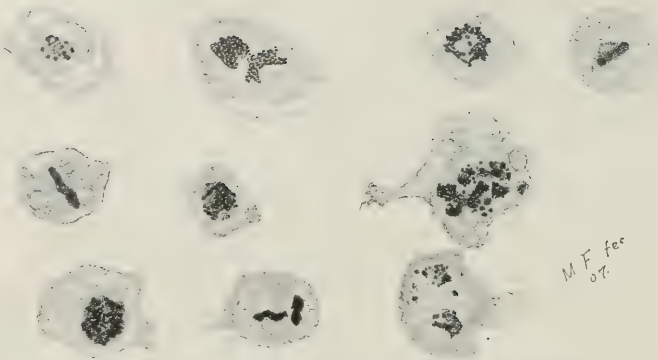

FIG. 4.—Camera lucida drawing of individual cells showing nuclear figures.

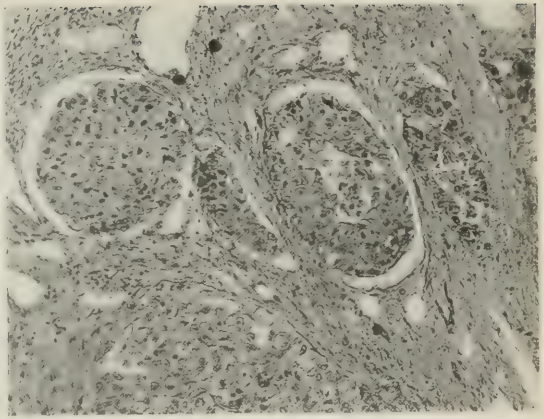

FIG. 5.—Photomicrograph. Portal vessels plugged by new growth. Cirrhotic liver.

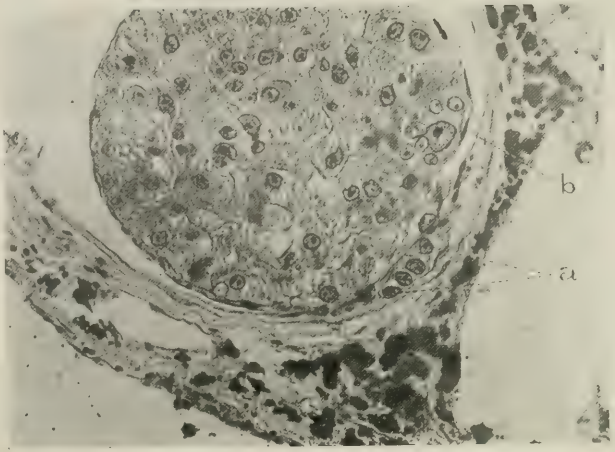

FIG. 6.—Photomicrograph. New growth plugging pulmonary vessel: (*a*) tumor cells invading vessel wall; (*b*) endothelial covering.

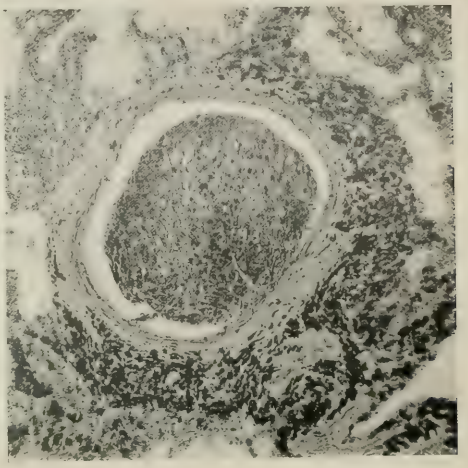

FIG. 7.—Photomicrograph. New growth plugging pulmonary vessel.

disclosed everywhere fine grayish white lines of irregular size and shape. At one point near the pleural surface of the right upper lobe were two small grayish white firm nodules 5-6 mm. in diameter, adjacent to each other. Minute dissection of the lungs failed to show any other nodules.

Microscopically, the blood vessels of the lungs were plugged for the most part by masses of cells similar to those described in the portal vessels and vena cava (Figs. 6 and 7). Mitotic figures were noted. The necrotic tissue in such a plug usually occupied the central portion, but might involve one side also. In some of the vessels the tumor cells had become a part of the vessel wall, the endothelial envelope having disappeared perhaps by a lateral necrosis as above described, and the endothelium of the vessel wall was reflected over the mass of tumor cells. Occasionally, an actual infiltration of the wall by tumor cells could be clearly demonstrated (Fig. 6).

The metastatic nodules were composed of new growth involving and filling the alveolar spaces; their walls gradually assuming the character of delicate connective-tissue septa between the masses of cells. Large areas of necrosis were present containing hyalined blood vessels. Serial sections demonstrated that these necrotic areas joined each other to form a thick worm-like mass evidently the original plug.

Several interesting points present themselves in this case, most of which have been reported in literature.

Although a careful search was made no primary focus in the gall bladder, stomach, pancreas, or rectum was found. Rolleston reported a case of secondary new growth in the liver due to primary lesion of the appendix. A primary lesion of the gastro-intestinal tract without manifestation followed by a metastasis in the liver might not be impossible, as secondary growths have been found in the inguinal glands due to continual irritation of the scrotum in chimney sweeps (Butlin). The age and sex of this case corresponds with the most frequent instances in statistics. The rather long duration of the symptoms has been emphasized in literature (White), though usually pain and more symptoms referable to a cirrhosis are present. The enlarged abdominal veins, œsophageal varices (post-mortem?) and ascites suggest the cirrhosis. Many cases of this disease have been complicated by a perihepatitis as well as gall stones. The relation of the latter to cancer has been much disputed, but properly should be discussed under cancer of the gall bladder. Although occurring frequently in primary cancer of the liver, it is generally considered a coincidence.

Aside from the general lesions which might be expected in a person of this age, the acute hæmorrhagic pancreatitis is the only unusual complication and has not been observed under similar conditions so far as I have been able to learn. The abdominal viscera were all much congested but otherwise no ætiological factor was found.

The liver in this case, as sometimes happens, was of about normal size and would not warrant a diagnosis of hobnail although the consistency proved undoubtedly that there was a rather marked degree of cirrhosis. No large tumor nodule was present and the relatively even size of the nodules would suggest multiple independent foci. The causes of such a tumor, which we will take up in a moment, would be consistent with this view, but to me it seems more probable that a larger part of the nodules must be of secondary origin; the relative ages being apparently so different. It is asserted that even the multiple foci are merely secondary tumors from a primary focus and that the comparatively rapid development of the metastatic growths gives them all a picture of similar age. In this liver there were several small nodules, which, by mitotic figures, and markedly compressed liver tissue about the periphery, denoted their rapid growth. No umbilication was noted, which is the rule in these cases, the connective-tissue element being too insignificant to cause shrinking or contracting.

The right lobe is usually most involved though in the present case the central portion was also largely involved.

The liver tissue which occupied perhaps a third of the organ showed a well-marked intra-lobular cirrhosis in which proliferation of the bile ducts and regeneration were marked.

The nodules in what might be called an early stage were composed of spheroidal or hexagonal cells arranged in columns separated by capillaries. In such areas the element of connective tissue was practically nil. In other nodules, however, connective tissue was more evident, separating the columns into islands and nests of cells. In still other areas the strands of fibrous tissue were very marked and separated even individual cells, at times giving the appearance of the type known as diffuse carcinoma, but the prevailing structure was the one first described. Other arrangements of the tumor cells have been reported (Thomson, Travis).

The number of mitotic figures was quite remarkable, a fact upon which little emphasis is laid in literature. The chromatin was arranged in innumerable fantastic shapes. Occasionally, multinuclear cells were observed, due probably to this atypical mitosis but considered by some to be artefacts (Rolleston).

The invasion of the lymphatics and blood vessels seems to be an important characteristic of this type of tumor, and though no actual invasion was noted under the microscope in this case, it has been seen in other instances. Given an invasion of the portal system with new growth, the diffuse distribution throughout the liver is easily accounted for.

Metastases into the lungs, pleura, gastro-hepatic glands and peritoneum have all been reported, the first being the most common. The presence of cells in the portal vessels is not inconsistent with a benign adenoma, but infiltration of the vessel walls and metastasis proves the malignancy of the new growth at once. I have been unable to find a case in literature in which the inferior vena cava has been so extensively plugged. It is surprising that the circulatory disturbances were so slight. The straggling ends, and loose deposits in the pulmonary artery, demonstrate the origin and path of the cancer emboli to the lung capillaries.

In the lung their growth and invasion of the vessel walls were easily seen. The necrotic areas of the metastatic

nodules which from serial sections evidently were parts of a former embolus of a vessel, suggests the earlier picture on which a metastasis has been built.

A word as to the origin of such a lesion. Various views have been set forth as to how cancer occurs aside from the general ætiology of cancer formation. In this type of case at least we have a true cirrhosis associated (Hanot), and the question arises as to what part it may play in the production of cancer. By some it is regarded merely as a coincidence (Thomson), but Muir, among others, affirms that it occurs much too often to be so considered. The cancer might be primary, with a cirrhosis resulting, but this is not borne out in cases of secondary carcinoma (Lancereaux). Eminent authorities as Hanot, and Gilbert consider that cancer and cirrhosis are together the result of some irritant, the nature of which we do not know, which works equally on the liver cells and connective-tissue cells, causing carcinoma and cirrhosis, respectively, or only one, in which case the other picture is lacking. They naïvely remark that cancer is produced much less often than cirrhosis. The more general view, however, at present seems to be that the cirrhosis is a distinctly old process on which a carcinomatous picture is superimposed. In a liver which is undergoing rapid regeneration it is not improbable that under certain conditions a compensatory hyperplasia might become atypical and assume the characteristics of a new growth. There are still those who maintain that the cancer develops directly from the liver cells (Hanot, Hunter), but equally good authorities consider there is an indirect step, the tumor cells arising from the cells of the compensatory hypertrophy (Rohwetter). This seems to be borne out by history, and morbid anatomy (Eggel).

There is a certain analogy between this condition and a chronic endarteritis which defeats itself. The occurrence of cancer in a cirrhotic liver has its analogy in the cancer developing in a chronic interstitial mastitis.

Cohnheim's views on the ætiology of cancer have to be considered and embryonic remains such as a duodenal diverticulum or an aberrant suprarenal must be thought of.

In the case here described the tumor cells resemble more closely the regenerated cells at least in respect to their nuclei, and the transition from regenerated cells to tumor cells seems less marked, though the types of cell could be differentiated without much difficulty.

On the whole, it seems as if the cancer in this type of liver was "due to an acquired habit of proliferation of the liver cells which starting as a compensatory hyperplasia gives rise to multiple adenomata eventually becoming so extensive as to constitute the cancer" (Rolleston).

The ætiology of this enormous unlimited growth of the cancer cells still remains a problem.

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A STUDY OF THE ANATOMICAL RELATIONS IN A CONGENITAL CYSTIC KIDNEY.

By F. M. Meader.

(From the Pathological Laboratory, Johns Hopkins University.)

This study is to determine the relation of the cavities in a congenital cystic kidney to the glomeruli and convoluted tubules. The material is from a fœtus described recently by Dr. Frank W. Lynch,[1] of Chicago. In so far as it illuminates our problem we shall draw postmortem details from this report. The case was pointed out by Dr. MacCallum as being suitable for our purpose; first, because of the early stage in development; second, because of the uniformly small size of the cysts.

[1] Dystocia from Congenital Cystic Kidney of the Fœtus. By Frank W. Lynch. Jour. of Surgery, Gynecology and Obstetrics, Vol. III.

The fœtus is from the fourth confinement of a colored woman twenty-six years of age. Her three children are healthy, the eldest is six years of age and the youngest three years. Twins were born at this confinement. The first that presented, the one in which we are interested, was a male, and born dead, the other was a female and lived. The dead fœtus measured 42 cm. in length and weighed 3800 grams. A meningocele 4 x 3 x 2 cm. in size protruded from the posterior fontanelle. There were sixteen teeth which were distinctly marked off and were cartilaginous in consistency. The hands were deformed; the left had a thumb and five fingers, the right had a thumb and five fingers and extending from the

FIG. 1.

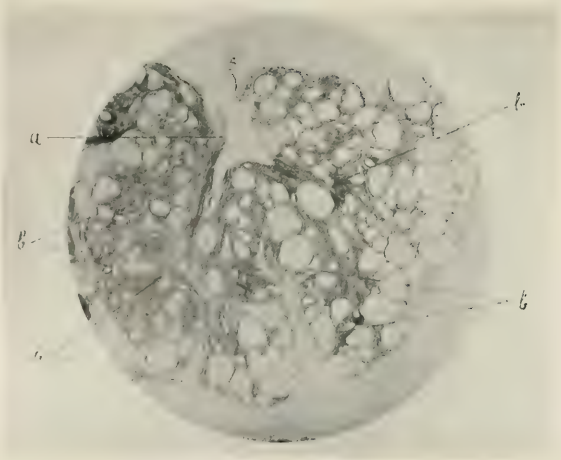

FIG. 2.

FIG. 3.

palmar surface of the little finger was an accessory finger. The feet were clubbed, presenting six toes on the right and seven on the left foot.

At autopsy Dr. Lynch states that there were no abnormalities save in the liver, kidneys, ureter and bladder. The liver was cystic. The left kidney was converted into a cystic mass which weighed 1190 grams. Externally, the kidney was divided into a number of irregular areas, some of them distinctly cystic (Fig. 1).

The capsule peeled off easily. On section the kidney was semi-solid and was found to be composed of myriads of cysts, which ranged in size from several centimeters in diameter to those so small as to be perceived with difficulty. The fluid obtained from the larger cysts was of a clear serous character. The ureter was attached to the middle of the posterior portion of the tumor. At the junction with the kidney, the ureter was 1.5 mm. in diameter, and presented a patulous lumen. The right kidney was represented by a collapsed sac 13 x 7 x 4 cm. Its exterior was generally smooth, while the interior was lined by a glistening corrugated membrane, giving a honey-comb appearance. The wall of the sac measured but 2 mm. in thickness. The ureter was kinked and stenosed a few centimeters above the bladder. The bladder was empty.

The kidney was cut coronally, and half of it was hardened in Zenker's fluid, and embedded in celloidin. The other half was preserved in formalin and used as a museum specimen. Its photograph is presented in Fig. 1. A portion from the surface of the embedded material was cut 25 m. in thickness and mounted serially. Among others, a series of cysts along the course of a blood vessel was studied. In order to make the relations precise a wax model of the blood vessel and its cysts was made. In Fig. 3 the blood vessel is represented in white and the cysts in black and the numerous glomeruli are indicated by labels. The model was made 100 times the actual size. In order to study the deeper cysts, especially those near the pelvis, the remaining embedded mass was cut 75 μ in thickness and mounted serially. This also enabled us to study the coarser architecture of the kidney.

The external malformations of the fœtus suggest at once that the kidney may have structural defects, and it is found that the cortex is thickened to comprise the bulk of the kidney, while the medullary portion is entirely absent. Glomeruli are found near the calyces of the pelvis which is contiguous to the under surface of the cortex (Fig. 1). From the pelvis of the kidney thick partitions of embryonic connective tissue extend toward the surface (Fig. 2). Between these partitions may be found cone shaped or pyramidal packets (Fig. 2), surrounded by connective tissue, some of which extend with their apex toward the pelvis and base toward the surface, while others extend in the reverse direction. In the apex and for some distance down the side of the packet may be seen numerous glomeruli. About one hundred glomeruli were observed on the walls of one packet. As the tubules approach the base of the packet they increase in size and decrease in number.

The relation of the cysts to the glomeruli as found in different parts of the cortex is very interesting. Occasionally a cyst is found which has a glomerular tuft hanging from its lining wall. Clearly such a cyst is a dilatation of the capsule of the glomerulus. Frequently one found the dilatation to occur in the first convoluted tubule, while the glomerulus is normal and connected with the cyst by the proximal part of the tubule. Sometimes two kinds of cysts are connected by a small tubule (Fig. 3). There is a relatively small dilatation of the glomerular capsule which is connected by a narrow tubule with a large dilatation of the first convoluted tubule. Occasionally the glomerulus is flattened out into a tubular body, closely surrounded by its capsule, and by a slender tubule this glomerulus communicates with a relatively small cyst. Again there are numerous glomeruli with no cysts, nor even any uriniferous tubule. The glomeruli vary extensively in size. When a glomerulus is connected with a cyst at all it is found that a large glomerulus accompanies a large cyst. There was never more than one glomerulus connected with each cyst. The largest cysts have no opening whatsoever, nor have they any glomeruli, although it seems possible that their glomeruli have degenerated.

The blood vessels are not very numerous. The arteries are quite large and their walls are extensively thickened. The efferent vessels are very difficult to follow.

We were unable to find a cyst that communicated with the pelvis. In fact on dissection, the walls of the calyces were glued together so that such communication would have been quite impossible.

Some of the cysts were filled with a colloid like substance, which frequently becomes lost in making the section.

The walls of the tubules and cysts are generally lined with a single layer of cubical epithelium. In some places the epithelium is necrotic and has disappeared.

In concluding this study we might review in detail the various hypotheses which have been promulgated to explain the formation of these cysts. But these views have been so ably presented in the recent literature on this subject that our facts may be merely restated and the simplest explanation attempted.

We have a kidney which has evidently suffered disturbances in the course of its development analogous to those which produced such changes in the limbs and head. It could never have performed its proper functions for the bladder was empty and the pelvis of the kidney obliterated, and in the kidney itself the connections of the various portions of the secreting tubules are especially distorted. We find glomeruli without uriniferous tubules, glomeruli with dilated capsule but with no outlet, glomeruli opening into a short uriniferous tubule which ends in a cyst, and finally similar glomeruli connected by a tubule with a cyst, but the Bowman's capsule of which is itself dilated into a second cyst. Each cyst has only a single associated glomerulus, but there are certain large cysts, about which no remains of a glomerulus can be traced. No light is thrown on the mechanism of these changes, but the reconstruction in wax serves to make clear the nature of the anatomical relations in the kidney.

PHLEGMONOUS GASTRITIS.

By A. B. Cecil.

(From the Pathological Laboratory, Johns Hopkins Medical School.)

Phlegmonous gastritis or suppurative inflammation of the stomach wall may be diffuse or circumscribed affecting in both instances especially the submucosa. In the circumscribed form there may be a clearly defined tumor-like abscess set as it were in the submucous coat and varying in size from that of a hazel nut to that of an orange. In the diffuse form on the other hand a large part of the stomach wall becomes extraordinarily thickened by the infiltration of the layers and especially the submucosa with a purulent exudate. These conditions are regarded as primary in the stomach when no extensive area of infection elsewhere makes it probable that they are metastatic in origin. Usually the ordinary pyogenic organisms are concerned as the cause.

The diffuse form is more common than the circumscribed but both are rare. The first case described was of the circumscribed form observed by Varandaeus in 1620. The diffuse form was not described until about one hundred and fifty years later, when a case was studied by Andral and Cruveilhier. Since then a number of cases have been recorded and the literature reviewed by Raynaud (1861), Auvray (1866), Lowenstein (1874), Leube (1876), Glax (1884), Oser (1887), Ruking (1890), Mintz (1892), and more recently by Leith who brings it up to 1896 in an excellent article.[1] At the suggestion of Dr. MacCallum the remaining cases up to the present time have been reviewed using Leith's paper as a starting point with finally a description of the case which recently came under observation at the Johns Hopkins Hospital. The following cases have been described since 1896 and their characters will afford a general idea as to the nature of the process as a whole:

Huguenin.[2]—Painter, aged 73, illness began with attacks of pain in stomach, belching but no vomiting, pulse and temperature low; during the 11 days of illness the temperature gradually rose to 38.8° C.

At autopsy the peritoneum contained a purulent fluid with fibrin. Stomach presented a network of lymphatics distended with pus. Mucosa uniformly grayish. An old ulcer with thrombosed vessels on lesser curvature. Stomach wall markedly thickened, especially in region of the ulcer, the submucosa and musculature being especially thick and on pressure pus oozes out from them, in which streptococci are found.

The author believes that the chronic ulcer formed a portal of entry for streptococci and that the chronic gastritis weakened the activity of the gastric juice and thus allowed the bacteria to grow and invade.

Hopkins and Weir.[3]—Male, aged 38. Complained of pain and epigastric tenderness, vomiting of bile-stained matter. Temperature reached 104° F., pulse 120, feeble and thin. Symptoms of peritonitis preceded death.

Peritoneum contained a purulent fluid. Stomach wall greatly thickened in pyloric region and from there for about one-third of its length by the accumulation of a purulent exudate chiefly in the submucosa. There was no ulceration, but in the lesser curvature were two small abscesses which had penetrated to the peritoneum. Diplococci and bacilli were found in the inflamed tissue.

Hueter.[4]—Man, aged 61. Sick only a few hours with diarrhœa and vomiting and slight fever.

At autopsy there was a beginning peritonitis. The stomach greatly distended and roughened by fibrin. The stomach wall was greatly thickened, especially along the greater curvature, purulent fluid may be squeezed from the thickened submucosa and is found to contain cells which stain badly and streptococci together with other bacteria. There were two small ulcers along the lesser curvature and some hæmorrhagic erosions in the pyloric region which may have acted as portals of entry. In many places the mucosa and musculature are necrotic.

Merkel.[5]—Woman, aged 45, with leukæmia treated by X-rays. At autopsy peritoneal cavity full of cloudy fluid and lined by fibrino-purulent exudate. Omentum thick and swollen. Spleen greatly enlarged. Fibrinous exudate over stomach. Fundus is normal, but the remainder is greatly thickened and doughy. Submucosa thickly infiltrated with purulent exudate laden with streptococci. Most marked infiltration was near the pyloric ring where there was a punched out round ulcer which probably acted as portal of entry for the bacteria.

Klienberger.[6]—Man, aged 67, treated with iodides and calomel for various troubles. Vomiting, diarrhœa, and epigastric tenderness, later constipation during two days when death occurred. At autopsy there was general peritonitis. Omentum adherent to pylorus and infiltrated with pus. Stomach wall is everywhere about 1.5 cm. in thickness and uniformly infiltrated with pus, except for certain small abscesses in folds of the mucosa. This infiltration contains Gram staining cocci and Weigert's stain of sections shows bacteria in masses often intracellular. Author believes the iodides and calomel caused irritation of stomach and lowered resistance.

McKenzie.[7]—Male, aged 28. Abdominal and thoracic chest pain, nausea, no abdominal tenderness, purplish blotches over body, fever, rapid respiration, vomiting. Later great abdominal pain, tense walls, general collapse.

At autopsy peritoneal cavity contained purulent fluid. Stomach wall thickened and soft, 1.4 cm. in thickness, purulent fluid oozed from submucosa. Mucosa mottled with pink and yellow patches, lymphatics filled with purulent fluid. The infiltration of purulent exudate involves mucosa and muscularis, but to a far greater extent the submucosa. It extends a short way into the duodenum. Cultures from stomach wall and peritoneum showed Staphylococcus aureus. Author thinks the ætiological factor a gastro-intestinal infection from bad meat.

C. J. Wagner.[8]—Man, aged 30. Chills, nausea, and pain in stomach sharply localized. Vomiting, fever, rapid pulse, collapse, and death on 10th day. Autopsy showed acute fibrino-purulent peritonitis, most intense over anterior surface of stomach, no perforation, stomach large and heavy. The wall measures 1.3 cm. in thickness and creamy pus could be squeezed from the

[1] Edinburgh Med. Jour., Vol. XLI.
[2] Rev. Med. d. la Suisse Romande, 1903, XXIII, p. 727.
[3] Brit. Med. Journ., 1904, Vol. II, p. 1406.
[4] Münch. Med. Woch., 1904, p. 85.
[5] Centralbl. f. Med. Wiss. No. 10, 1905, p. 257.
[6] Münch. Med. Woch., 1903, p. 1338.
[7] Canada Lancet, February, 1907.
[8] Canadian Pract. and Review, January, 1907, p. 12.

submucosa. Mucosa congested with superficial ulcers and infiltrated with leucocytes. Musculature and subserous tissues also infiltrated. Streptococci and bacilli found in smears. Cultures showed only B. coli and B. proteus.

SCHARROZ.[9]—Man, aged 59. No clinical history. Fresh diffuse peritonitis was found at autopsy. Stomach wall thickened to 2 cm. in pyloric region. Submucosa and musculature formed a broad homogeneous light yellow layer from which thick creamy pus oozes. Mucosa reddened and swollen, but without ulceration. Author thinks infection occurred from the tonsils, since cultures from stomach, peritoneum, and tonsils gave streptococci.

SCHMIDT.[10]—Woman, aged 70. At autopsy there was found a purulent peritonitis. There was a purulent infiltration of the submucosa of the stomach, the lymphatics being filled with exudate. There was no perforation of gastric wall, but infection extended along the lymphatics which were elevated in thick yellow wreaths. Mucosa not affected. Cultures from the submucosa and peritoneal exudate showed streptococci. Author thinks infection occurred through the mucosa although the portal of entry cannot be determined.

KONSTANTINOVITCH.[11] I. Woman, 41 years old. Fever, chill, malaise, abdominal pain, vomiting, rapid small pulse, abdomen distended and tense.

At autopsy purulent peritonitis especially about stomach. Peritoneal coat of stomach injected and through it there shine yellow opaque spots. Stomach enlarged, mucosa swollen and œdematous with many hæmorrhages. Walls much thickened from infiltration of submucosa.

Microscopically this purulent infiltration is found to invade mucosa and musculature. Veins thrombosed. Streptococci found in the stomach walls.

II. Man, aged 23. Malaise, abdominal pain, tendency to vomiting and diarrhœa, fever, rapid respiration and abdominal tenderness. Operation after seven days revealed hæmorrhagic peritonitis with gluing together of intestine.

Autopsy revealed general peritonitis. Stomach enlarged, serosa covered with exudate. Mucosa swollen and covered with punctiform hæmorrhages and shows several defects from which pus oozes. Wall of stomach thickened (1 cm.). Submucosa especially infiltrated with pus. Streptococci were found in the wall. Author believes they can invade through the mucosa even without defects of its tissue.

MAX JACOBY.[12]—I. Man, aged 24. Ill for 12 days before death. Abdominal pain, headache, diarrhœa, tympanites. No fever, intellect clouded. Right thigh hard, tender, and livid.

At autopsy a litre of yellow pus was found in peritoneum. Intestines injected and glued together by fibrino-purulent exudate. Pylorus narrow, near it the scar of an old ulcer. Stomach wall much thickened by purulent exudate which is particularly abundant about the ulcer where the wall measures 1½ cm. of which 1 cm. is occupied by the submucosa from which a purulent fluid oozes. Muscular and subserous tissue also infiltrated. Scattered over the mucosa there are several punctiform defects. Streptococci found in stomach wall and in muscles of thigh. Cultures showed streptococcus, B. coli, and B. proteus.

II. Woman, aged 24. Pain in gastric region, vomiting of coffee ground material. Abdominal tenderness, palpable tumor in midline above umbilicus. No fever, exploratory laparotomy and gastro enterostomy; death after illness of 8 days.

Autopsy.—Peritoneal cavity contained 1 litre of pus. Stomach enlarged at pylorus, a hard nodular tumor which proved to be a round ulcer 6 x 9 cm., small defects in its otherwise smooth base. Extending from the ulcer a diffuse thickening of the stomach wall due especially to infiltration of the submucosa from which pus could be squeezed. Muscular and subserous tissues also affected. Mucosa swollen with ecchymoses. Streptococci found in stomach wall. Author thinks that the phlegmonous gastritis resulted from the operation which was performed 6 days before death.

KINNICUTT.[13]—Man, aged 41. Drunken bout, vomiting, abdominal pain, fever, shallow respiration, abdominal tenderness.

At autopsy a sero-fibrinous peritonitis. Stomach wall greatly thickened by a purulent infiltration of the submucosa. A necrotic patch was found in a cicatrix near pylorus which was possibly the portal of entry of the streptococci which were abundant.

SIMMONS.[14]—Woman, aged 75. High fever and abdominal pain, death next day. At autopsy stomach wall was found greatly thickened by an infiltration of the submucosa with cloudy serous and purulent fluid, mucosa swollen but without defects. There was bronchiectasis and thrombosis of the crural veins and streptococci were found in these localities as well as in the stomach wall. Author thinks the bronchial infection primary.

CAYLEY.[15]—Woman, aged 26. Chills, headache, pain in abdomen, vomiting, constipation, fever, and rapid pulse. Abdominal tenderness, collapse and death. Autopsy revealed general purulent peritonitis. Stomach wall thickened by infiltration of submucosa, muscularis, and subserosa, smears showed streptococci and a bacillus not staining by Gram's method. Cultures show B. coli and streptococcus.

From these cases it is seen that while in some instances it is impossible to trace the mode of infection there is often an obvious source of the organisms and an equally obvious defect of the tissues of the stomach wall which might allow their invasion.

The case which occurred in this hospital recently resembles the above very closely and adds little new light to the understanding of the condition, but it may be reported on account of the relative rarity of such cases.

The clinical history obtained after death of the patient from the parents was as follows:

BERTIE H.—Female. Aged 25. Family history unimportant.

Personal History.—For past two years patient has had "muscular rheumatism" with pains in the joints and muscles at times, and for about a year has complained of pain in epigastric region and in back which comes on only after eating and lasts only a short while. Constipation, but no history of nausea or vomiting.

Eight days before death the patient went down the bay in a boat. She had not felt well for about a month, complaining especially of the pain in stomach and back. On getting home that night she vomited a quantity of greenish fluid, and went to bed complaining of severe pain in abdomen. Vomiting continued and became very frequent, vomitus was a yellow fæculent, very offensive fluid. Abdomen became extremely sensitive. Diarrhœa began and there were very frequent evacuations. Patient ate nothing, complained at times of pain. She was brought into the hospital much distended and suffering excessively from pain and tenderness in the abdomen. An exploratory laparotomy by Dr. Casler revealed an abscess between the stomach and the liver with a good deal of matting together of the intestinal loops about this area. The abscess was drained, but the patient died an hour or two later.

Autopsy 10 hours after death. Autopsy 2901.

Anatomical diagnosis.—Phlegmonous gastritis; localized peri-

[9] Wien. Med. Woch., 1905, p. 904.

[10] Dtsch. Med. Woch., 1905, XXXI, p. 287.

[11] Centralbl. f. Stoffwechsel M. Verdauungs Krankheiten. Göttingen, 1903, IV, p. 295.

[12] Ueber Gastritis Phlegmonosa, 1899.

[13] Phila. Med. Journ., 1900, V, p. 989.

[14] Münch. Med. Woch., 1901, XLVIII, p. 440.

[15] Trans. Path. Soc. London, 1902, LIII. p. 282.

tonitis and abscess formation; acute splenic tumor; degenerative changes in the liver and kidneys; lobular pneumonia; chronic adhesive pleuritis and pericarditis. Body is that of a well built negro woman. Through a long abdominal incision in the median line a drain runs down to an inflamed area in the upper abdomen. The omentum is much thickened and bound to the liver by adhesions. The peritoneum in general contains no excess of fluid. The surfaces are smooth. The stomach lies below the liver, is pale and greenish with small hæmorrhages upon its surface here and there. The abscess which was drained lay in front of the stomach above its pyloric portion bounded above and toward the median line by the liver, and matted tissues about the round ligament. The lymph glands in this region are markedly enlarged. Between the stomach and the liver which are adherent to one another, there is a second abscess cavity filled with thick turbid fluid. The pancreas is normal and there are no fat necroses. The mucosa of the duodenum is normal, and the common bile duct and pancreatic duct show no alteration. The Brunner's glands are prominent up to the normal pylorus. The stomach is not distended. Its surface is roughened by fibrin with flecks of hæmorrhage. For a distance of 1 cm. above the pylorus the mucosa is folded and easily movable. Above this it is stretched tightly over the swollen underlying tissue and cannot be moved. Throughout an area which extends for a distance of 10 cm. and involves the whole circumference of the stomach, the gastric wall measures 12 mm. in thickness. At its thickest part it is not very firm, but rather boggy, being softer in some places than in others. On the cut edge of the stomach wall the muscle layer is very distinctly visible and has a translucent greenish appearance. The subserous tissue is more opaque and dull looking, and is slightly thickened, but the submucosa is enormously tickened. It is moist, dull yellowish green and rather opaque, with slightly injected minute vessels. The injection is relatively very slight and a turbid greenish fluid exudes from the cut surface. The mucosa does not seem particularly thickened, although it is rather moist and swollen looking. There are no ulcerations visible, but minute white spots with a darker centre are scattered over its surface and are probably lymphoid nodules. The remainder of the gastric mucosa is practically normal in appearance, except for a few minute hæmorrhages. The lymph glands in the neighborhood of the stomach are opaque and swollen, and those about the head of the pancreas are particularly enlarged.

Pancreas is normal. The *spleen* is much enlarged, weighs 200 gms. The Malpighian bodies are greatly enlarged. The pulp is opaque grayish red. The *liver* weighs 1900 gms. and is of an opaque ochre yellow color. The lobules are very much swollen and very dull and opaque looking. The *kidneys* are not enlarged, they show a similar opacity in their cortex, but are otherwise normal. The remaining abdominal organs show no special abnormality. In the thorax the *lungs* are bound to the costal pleura by firm adhesions. The pericardial cavity is obliterated by similar adhesions. The *heart* is somewhat enlarged. The lungs are hyperæmic and show lobular patches of consolidation scattered throughout them.

The microscopical examination of the stomach shows that the thickening of the stomach wall is due to an extraordinary infiltration with a purulent exudate. The mucosa is practically normal, there being only a slight abrasion of cells from the most superficial portions of the glands. There is a slight infiltration of the muscularis mucosa, but beneath this the submucosa is rendered unrecognizable by the very wide separation of its tissue elements by the exudate. The blood vessels are spread wide apart and many of them are thrombosed. The lymphatics are enormously distended with fluid and cells. The connective tissue fibres are spread wide apart by the exudate which consists of fluid, fibrin and leucocytes. The fibrin forms a very delicate network. The cellular elements are for the most part polymorphonuclear leucocytes, but there are also some mononuclear cells; most of them are fairly well preserved, but in places they have lost their nuclei and are disintegrated. Where the cells are most closely packed the disintegration is most marked and here apparently the bacteria are collected in the greatest abundance. The muscularis is also greatly thickened by the separation of the muscle bundles by quantities of fluid, fibrin, and leucocytes. The exudate is here of quite the same character as in the submucosa and extends through to the subserous tissue which is also much thickened and is limited by a dull layer of fibrin which covers its peritoneal surface. (Fig. 1.)

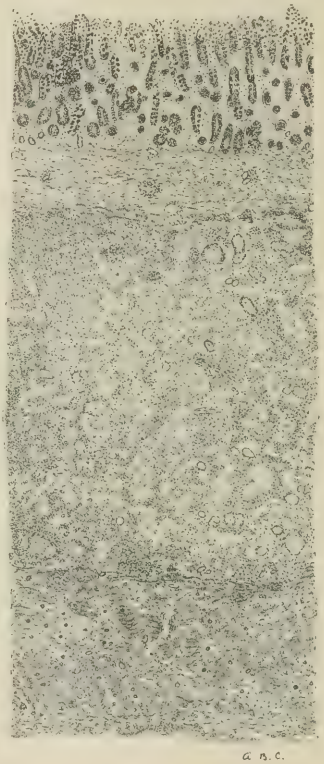

Fig. 1.—Section of stomach wall. Prepyloric portion of greater curvature.

Bacteriological examination.—Smears were made from the purulent fluid oozing from the stomach wall and stained by various methods. These smears show a number of bacilli, usually in pairs together with a much larger number of smaller organisms, somewhat lanceolate in form about the size of the pneumococcus and occurring in pairs. These stain very badly and many of them seem to be mere shells, in other instances they look like bacilli with polar staining, and a clear space in the centre. The paired bacilli described are quite stout and stain very brilliantly. Sections of the stomach wall stained by Weigert's method show only one type of organism, but those are present in enormous numbers, both inside the leucocytes and free. These stain well for the most part, but some of them are mere shadows as seen in the smears. They are diplococcus forms, sometimes somewhat lanceolate in form, sometimes almost like short bacilli. In some instances the resemblance to a polar staining bacillus is again

evident. No large bacilli are seen in the sections stained by Weigert's method. No chains of cocci nor clumps can be made out. They are practically always in pairs. Cultures were made with extreme care from the stomach wall upon agar and in bouillon, but the colonies which appeared proved on examination to be colonies of the Bacillus coli communis. There are one or two colonies of a non-Gram staining sarcina, but no colonies of cocci appeared. Several of the plates showed only uniform colonies of the Bacillus coli communis. It is extremely unfortunate that the bacteriological study is so unsatisfactory in spite of the care taken to make successful cultures. It seems probable that the colon bacilli were secondary invaders, and that the coccus forms which failed to grow in the cultures formed the actual causative factor.

ON THE OCCURRENCE AND PHYSIOLOGICAL NATURE OF GLANDULAR HYPERPLASIA OF THE THYROID (DOG AND SHEEP), TOGETHER WITH REMARKS ON IMPORTANT CLINICAL (HUMAN) PROBLEMS.[1]

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INTRODUCTION.

In taking up the study of so complex a problem as goitre, it seemed to me that human material could not be given primary consideration on account of the maze of complicating and perplexing conditions through which to interpret one's observations.

The dog and sheep were chosen as the animals most suited for the study of fundamental problems for the following reasons: They offer abundant and readily accessible material, complicating conditions are reduced to a minimum, experimental control is easily maintained, and lastly, as regards their food, these animals represent types to which man is intermediate. The next step was to establish a point of departure—a base line so as to speak. For this purpose *anatomy* seemed to offer the most satisfactory and constant base. My material has thus far consisted of 352 dogs' thyroids and parathyroids, 35 sheeps' thyroids, 31 bovine thyroids, and 173 human autopsy specimens, and preparations from as many other animals as opportunity afforded.

Concerning the term "Glandular Hyperplasia"—exactly what is meant? It is a descriptive term not susceptible of so varied an interpretation as is the term "Goitre," and by it is meant the occurrence of all grades of changes in the thyroid characterized by the production of columnar types of epithelium with the intra-acinar, papillomatous invaginations, by the hypertrophy of the stroma, by the increase in the blood-supply, and by a decrease in the stainable colloid. It may or may not be (as the name implies it generally is) associated with the formation of new acini. There are all grades of these changes ranging from the normal cubical gland cells to that stage where there is no longer any resemblance to thyroid at all, sections appearing as solid epithelial fields without acinar lumen or colloid. Histologically it is the same condition that Halsted (1) produced in normal dogs' thyroids by partial excision and which has been fully described by him and Welch (2).

DISTRIBUTION AND INCIDENCE.

This condition of the thyroid is spoken of by the physicians and laymen as Goitre. It is one phase or stage of goitre. It is very common (endemic) throughout the region of the Great Lakes from Montreal to Duluth (3, 4, 5), though its incidence, clinically at least, varies in the different districts, *e. g.*, in Buffalo and Detroit one sees a greater proportion of the animals affected than in Chicago. In the district of Cleveland about 90 per cent of all the street dogs show the glandular changes on histological examination. Sheep are affected to about the same extent, especially in the Lake Erie slope of Michigan and Ohio. Cattle are affected but apparently to a lesser extent. Exact limitations of this area are important, particularly to ascertain whether it is confined to the region of glacial drift or not. Clinically at least goitre is diminishing in frequency in the region of the Lakes as is true in all goitrous districts (6, 7). This is especially true of the sheep in Michigan, where some 15 to 20 years ago the future of the industry was a serious consideration on account of the number of cretin lambs, but now it is gradually disappearing. Acclimation and the more extensive use of iodine-containing salt have undoubtedly been great factors in its disappearance. Well cared-for dogs show a greatly lessened percentage of glandular hyperplasias. Of the animals below the mammalia, I am not prepared to make a statement.

ANATOMICAL DESCRIPTIONS.[2]

(1) *The normal gland* for all mammalia shows only minor histological differences—the herbivora generally having a more prominent stroma. In the dog the normal gland does not exceed 0.300 gm. per kg. of body weight. The gland capsule is thin. The vessels are small. In color the gland is pale, yellowish-gray, and translucent. On section it is firm, rubbery, and one can see the acini filled with clear honey-colored colloid of a thick syrupy consistency. Microscopically the acini are rounded, slightly variable in size and with regular walls. There are no intra-acinar twigs or pro-

[1] Presented at the meeting of the American Association of Pathologists and Bacteriologists, May 9, 1907, by Dr. R. G. Perkins.

[2] Technique: In all the histological work four per cent formaldehyde solution has been used as the hardening reagent because the metallic salts so fix the colloid as to render sectioning at 10 to 15 microns with the celloidin method very difficult. The tissues were imbedded in celloidin and the sections were stained in Delafield's hæmatoxylin and two per cent yellow eosin.

jections. The stroma is scanty and supports very small blood- and lymph-vessels. The epithelial cells lining the acini are regular, low cubical, with small darkly staining nuclei, and are arranged in a single layer. The stainable colloid is dense, homogeneous and stains uniformly. It sharply abuts on the epithelial cells. Adjoining acini may show colloid of different staining intensity—a condition that has been attributed to a possible variation in the lymphatic drainage.

(2) *The glandular hyperplasias.*[3]—Here the changes are similar to those occurring in primary (exophthalmic) toxic goitre in man and are identical with those described by Halsted (8) following partial excisions of normal dogs' thyroids. Of this type, as mentioned above, there are all graduations from the normal gland to the most extreme change in which there is no resemblance to thyroid at all.

This change may be briefly described as follows: The gland in the main shows enlargement proportional to the degree of glandular hyperplasia. In a moderate example, the thyroid lobes are enlarged uniformly and symmetrically. The capsule is thick and the vessels are much enlarged and tortuous. The lymphatic trunks leaving the gland are enlarged and if exposed during life are most striking for their size, and are filled with rather clear lymph-like fluid. On section the tissue is very vascular. It has a fleshy, opaque, gray-red appearance and a finely granular cut surface. There is no visible colloid. Microscopically the stainable colloid is greatly reduced or absent, there being in its place only a small amount of pink granular material. The acini show extensive papillomatous ingrowths and invaginations of their lining epithelium, more or less effacing the acinar lumina. The epithelium is high columnar in type and arranged in a single layer. The epithelial nuclei are large, pale, round, vesicular, and basal. The cytoplasm is quite granular. The stroma is diffusely increased, contains numerous, large blood and lymph channels and occasional small collections of lymphoid cells.

(3) *Simple colloid goitre.*—The changes noted in uncomplicated forms are briefly as follows: Generally speaking they may be designated as exaggerations of the normal structures of a normal gland. There is uniform and symmetrical enlargement of the lobes. The capsule and blood-vessels are moderately enlarged and thickened, the blood-vessels as a rule showing very much thickened walls (a process of physiological obliterating endarteritis similar to that occurring in the involuting uterus), while the lymphatics are barely noticeable in the gross. On section the acini are large, well defined, and filled with dense uniform colloid with occasionally some blood pigment. (Hæmorrhage into the acini in the marked glandular hyperplasias is very common, and one frequently sees the surrounding epithelial cells filled with the blood pigment and it is not unlikely that the old pigment occasionally seen in the colloid stages represents the unabsorbed portion.) The tissue has a clear, translucent, yellow-gray appearance and is not vascular.

Microscopically the colloid stains uniformly and densely, and sharply abuts the epithelium. The acinar walls are often reduced to mere lines and in some glands there seems to be no increase in the inter-acinar framework—indeed it may seem diminished. In most colloid glands there are to be seen more or less numerous sprigs or twigs of acinar walls jutting into the acini, that are probably in part remnants of ruptured acinar walls, but, as will be shown later, are for the most part the remnants of the infoldings and invaginations of the epithelium as described under the glandular hyperplasias.

The following table of analysis of 202 dogs' thyroids gives a summary of the changes according to the structure and to the degree of change:

[3] While this paper deals particularly with the changes in the thyroid gland, it must be borne in mind that the animal, whether man, sheep, or dog, shows changes in other tissues that are equally as striking and are probably of equal importance.

These changes occur particularly in the lymphatic system, including the spleen and thymus, and are associated with varying degrees of chlorotic anæmia and changes in the blood picture.

In the case of the thymus, it is usually persistent and often enlarged. The spleen is also enlarged (in children frequently palpable) and histologically there is a general increase in the fibrous framework associated with great prominence of the Malpighian bodies. The lymph glands are universally enlarged, but show all degrees of hypertrophy from the slightest prominence to cases clinically simulating Hodgkin's disease as described by Warthin (9). Histologically they show a general increase in the stroma and also in the lymph-centres. The bone-marrow also shows changes of varying degrees that are not separable from those found in lymphatism. All these changes in the lymph and hæmatopœtic tissues are reflected in the blood picture. Dr. L. W. Ladd (10) tells me that for the human the main changes found in the blood are a reduction in the hæmoglobin and an absolute and a percentage increase in the mononuclear elements, which may be from 30 to 45 per cent of all white blood cells.

From this synopsis of the changes in other tissues, it can be seen that this subject has very important and intimate association with the condition called lymphatism or status lymphaticus on the one hand and with toxic (exophthalmic) goitre on the other. As is well known lymphatism shows distinct district limitations (Vienna, Cleveland) which for the most part are within the limits of endemic goitre. This leads to the question whether lymphatism should not represent a group of conditions characterized by varying degrees of lymphatic enlargement together with changes in the thyroid, occurring in animals, instead of being applied to those few individuals dying from some trivial cause, in which at post-mortem there is a persistence and marked hyperplasia of the lymphoid tissues. Then, too, a word as to syphilis in relation to this group of conditions. It is my opinion that syphilis has been unduly blamed for these changes in the human and that there is a great group of lymphatic enlargements in which syphilis plays no ætiological rôle whatever. This view is further strengthened by the fact that dogs, sheep, and cattle show the same changes that occur in man and iodine seems even more efficient in its treatment.

(It would be important to know whether iodine is stored in the lymph glands as well as in the thyroid and the thymus following its administration.)

TABLE OF ANALYSIS OF 202 DOGS' THYROIDS.[4]

Glands—size of:	
Normal	112
Slightly enlarged	52
Much enlarged	38
Capsule:	
Normal	108
Slightly thickened	61
Much thickened	33
Vessels:	
Normal	101
Slightly enlarged	66
Much enlarged	35
Stroma:	
Normal	64
Slightly increased	93
Much increased	45
Stainable colloid:	
Normal	49
Increased	18
Reduced (all degrees)	117
Absent	18
Alveoli:	
Normal	34
Distorted by papillomatous ingrowths—slight	45
moderate	44
marked	69
Increased in size	20
Alveolar epithelium:	
Normal (low cubical)	31
Uniform cubical	41
Low columnar	61
High columnar	69
Desquamation	33
Cell nuclei:	
Normal (small dark)	65
Moderate size, pale vesicular	19
Large size, pale vesicular	118
Glands—condition of:	
Normal	19
Colloid hypertrophy	15
Glandular hyperplasia (all degrees)	168

THE PHYSIOLOGICAL NATURE OF THE GLANDULAR HYPERPLASIAS.

From a careful study of the material, experimental and anatomical together with the available literature, I think the most rational conclusion is that it is a *physiological reaction* on the part of the gland to a demand from the tissues, and that these glandular changes are to be considered *cretinoid* in nature.

The following evidence may be cited:

(1) Clinically, dogs manifest all degrees of the symptom-group from true cretins to normal dogs.

(2) It affects the young and they tend to recover spontaneously.

(3) One can produce the same histological changes in puppies by partial removal of the glands from the mother before pregnancy.

(4) The same changes can be produced in normal dogs' thyroids by partial removal.

(5) The hyper-activity of the gland is evidenced by the tremendous increase in the blood-supply and the distended lymphatics.

(6) Anatomically there are all degrees of the reaction from the comparatively normal gland to the most marked glandular change. Taking up the assumption that these glandular changes represent stages in a physiological reaction to a deficiency as the most natural deduction from the observed phenomena, the question arose: What might this deficiency be, against which the gland was reacting? *Iodine* naturally was the first suggestion. The importance of iodine in the body economy is ill understood and I felt that further advance in the study of the thyroid would be hampered until the rôle and mode of action of iodine was better understood.

The fact that iodine is a normal constituent of the thyroid gland and that it is practically a specific remedy in endemic goitre suggests that it plays an important part in the normal physiological activity of the gland. In support of this view, the following data may be cited:

(1) The iodine content varies inversely with the degrees of glandular hyperplasia.

(2) Iodine or iodine containing compounds will reduce this glandular activity in the dog in all cases.

(3) Iodine will prevent the occurrence of glandular hyperplasia after partial removal of normal glands which would otherwise hypertrophy.

(4) Iodine will prevent the occurrence of hyperplasia of the thyroids of puppies from bitches in which three-fourths of the gland has been removed.

(5) Endemic hyperplasia of the thyroid does not occur along the seacoast. MacCallum (11) finds that about 7 per cent of the dogs' thyroids in Baltimore show glandular changes as compared with 90 per cent in Cleveland.

RELATION OF GLANDULAR HYPERPLASIA TO THE IODINE CONTENT.

It was early suspected that there might be a direct relationship, because Baumann (12) and Oswald (13) had shown that in general the iodine content varied directly with the amount of colloid (thyreo-globulin), and Oswald had further observed that in general the amount of stainable colloid varied inversely with the degree of glandular hyperplasia, therefore on these premises one could prophesy that the iodine content would vary inversely with the degree of glandular hyperplasia. This is exactly what is found to be the case. W. W. Williams (14) has shown that in general one can predict the condition of the epithelium from the iodine content of the gland. We have further shown that iodine is stored in the thyroid with great rapidity when fed to dogs and that it disappears from the gland very slowly.

EFFECT OF FEEDING IODINE CONTAINING COMPOUNDS ON THE THYROID GLAND AND ON THE ORGANISM AS A WHOLE.

The administration of iodine containing compounds to

[4] Cleveland Med. Journ., February, 1907.

dogs quickly (two to three weeks) induces a reversion of all the gland structures to a more normal type. I have followed this process step by step and parallel with the administration of known quantities of iodine, having first removed a control lobe from the dog and at intervals removing bits of the remaining lobe. The changes observed may be summarized as follows:

(1) Marked reduction in the size of the gland as a whole.

(2) Reduction in the blood-supply associated with obliterative endarteritic changes similar to those occurring in the uterine vessels during involution.

(3) The acinar epithelium reverts from high columnar to flat cubical. (This may take place in two weeks.)

(4) There is a rapid accumulation of normally staining colloid.

(5) There is a great increase in the iodine content of the gland over that of the control lobe and even over the normal content of a normal gland.

(6) The lymphatics instead of being the huge, sacculated trunks filled with rather clear watery fluid become barely noticeable.

The dogs' general condition undergoes equally striking changes. That is from a wizened, a sleepy, listless, rhachitic creature, he changes to an active, robust healthy dog.

Feeding fresh or desiccated sheeps' thyroids, however, often induces serious and toxic effects—a point that will be referred to later.

Relation of Iodine to the Body Economy.

The evidence brought out by the above experimental work, together with that found in the literature shows that iodine plays a remarkable rôle in the body metabolism (15). The work thus far does not exclude the possibility that iodine may be a specific remedy for an infecting agent operating in these cretinoid conditions. It does, I think, offer an adequate explanation on a physiological basis for all the observed phenomena.

Indeed there is reason to believe that the body economizes iodine much as it does iron, and to carry the suggestion further there is reason to believe that iodine is related to endemic goitre much as iron is to chlorosis. Both conditions are probably vastly complex, but these two elements (iodine and iron) may be the nuclei around which their metabolic complexities are grouped.

If iodine does play such an important rôle in the body metabolism its distribution in nature and in animal foods is important to ascertain. As to where this iodine deficiency exists I do not know. It might be in the food, in absorption, or in assimilation.

Relation of the Glandular Hyperplasias to Cretinism.

As before remarked I think the different degrees of glandular hyperplasia represent different stages or degrees in the cretinoid condition. The word "cretinoid" as used by Gull (16) is not exactly descriptive here, for while there is every reason to believe that these glands have a *hyposecretion* physiologically, yet *quantitatively they have a hypersecretion*, and this excess of an abnormal secretion produces certain toxic manifestations not unlike those seen in Graves' disease. If the deficiency is not met there is, as pointed out by Ord (17), a gradual destruction of the glandular tissue by fibrous overgrowth and subsequent loss of gland function.

Relation of Glandular Hyperplasia to Colloid Goitre.

The ease with which all cases of glandular hyperplasia in the dog revert to a colloid type upon the administration of iodine containing compounds suggests that colloid goitre is the quiescent stage. In other words, in its simplest form and conception, glandular hyperplasia is the hyperactive stage of the cells, and colloid goitre is the quiescent stage after the deficiency has been met. Whether this is the only mode of production of colloid goitre in the dog or sheep I do not know. It is the only form I have met with and certainly is the most important. It would seem that a purely passive dilatation of the acini would be possible, but for the determination of this point human colloid goitres could not be used because as we see them in the laboratory secondary changes or complications are present in all.

If this interpretation of the formation of colloid goitre be the correct or usual mode, then the term "colloid degeneration" as applied to colloid goitre is a misnomer.

Applications of These Findings to Important Clinical Problems.

Their bearing on the commercial preparations of the thyroid gland.—The nature of the active principle of the thyroid is, in all probability thyreo-globulin (colloid). This is the view advanced by Baumann (18), and Oswald's (19), Gauthier's (20), and Wells' (30) work upholds this view and it is accepted by most physiological chemists. As before mentioned, the iodine content varies directly with the amount of stainable colloid and also inversely with the degree of glandular hyperplasia in the dog and sheep. This being the case, desiccated thyroid made from these hyperplased sheeps' thyroids must also vary greatly in the amount of stainable (colloid) thyreo-globulin. Acting on this deduction I have found that these hyperplased sheeps' thyroids, whether fed fresh or dried, have a highly toxic action on cretin dogs. The main symptoms produced are: Increased appetite at first, rapid emaciation, progressive weakness, diarrhœa, tremor, and death. Normal dogs are more resistant. In feeding the commercial preparations, the same toxic effects are produced, but as a rule are less marked and different preparations show considerable variation in their toxic and their beneficial effects. I have lately had occasion to visit some of the larger commercial laboratories and find considerable difference of opinion as to normal and abnormal glands. In general the factories' "limit of normal" corresponds to the group of moderate glandular hyperplasia and generally the markedly enlarged glands are not used. The commercial preparations then contain a mixture of normal and abnormal glands and

may explain in part at least the great variation in activity clinically, and especially its generally injurious effects in the group of glandular hyperplasias in man and animals.

It is my belief that these hyperplased glands have a hypersecretion quantitatively, but that it is greatly altered, and is deficient in some important physiological constituent, and also has a highly toxic action.

(2) *Relation of the glandular hyperplasias to the thyroid in toxic (exophthalmic) goitre.*—There are some good reasons for believing that the disease in dogs, sheep, and cattle, characterized by hyperplasia of the thyroid with enlargement of the spleen; thymus and lymph glands are very closely related to toxic (exophthalmic) goitre in man.

For, aside from the occasional lesions found in the restiform body, medulla and cervical sympathetic, there are well refined and quite constant lesions, the most characteristic of which are glandular hyperplasia of the thyroid, persistence of the thymus as pointed out by Mackenzie (21), with enlargement of the spleen and lymph glands, thus bringing the lesions observed in animals to resemble very closely the lesions found in Graves' disease.

As pointed out before there is every reason to believe that these hyperplased glands have a hypersecretion quantitatively, but that physiologically it is deficient in some important constituent, and that this quantitative excess has a toxic action. The same conditions are observed in Graves' disease.

The belief has been expressed that these changes occurring in dog and sheep are to be considered cretinoid in nature, and it is my belief that further work will show a still closer relation between the glandular hyperplasias in animals and toxic (exophthalmic) goitre in man than I have indicated and that we shall recognize these changes as stages in the course toward myxœdema or cretinism. It is interesting to note that Ord (22), in 1898, wrote: "It appears to me probable that we shall recognize in the near future, more and more the occurrence of a stage of hypertrophy of the thyroid gland with or without the signs of Graves' disease as an antecedent of myxœdema." Howard (23) also has recently brought forward this idea with emphasis, and adds: "I believe that a history of exophthalmic goitre preceding the onset of myxœdema would be more frequently elicited if more careful inquiry were made." It might be pointed out here that myxœdema, according to case reports, rarely precedes, occasionally accompanies, and frequently follows the symptom-complex of Graves' disease.

This special phase of the subject is exceedingly important and no doubt it has been lost sight of largely through the hypersecretion theory of Gauthier (24), and Moebius (25). I am also inclined to think that the more we study toxic (exophthalmic) goitre, the more closely we shall find it related to the cretinoid condition of dog, sheep, and cattle; also that it is a reaction to a deficiency (29), and if the deficiency is met the gland reverts to a colloid type, and if not, the organism exhausts itself in the attempt to meet the deficiency but, to again quote Ord (26), "Such proliferation ending in the replacement of the true glandular structure by a fibrous material and consequent destruction of the function of the gland." Thus there is reason for believing that toxic (exophthalmic) goitre is a reaction to a deficiency and represents one step toward myxœdema, in which the true changes are masked by the toxic manifestations of an excessive secretion of toxic substance.

(3) *Relation of the glandular hyperplasias to ether anæsthesia.*—In the course of surgical work with dogs one can clearly notice distinct differences in the effect of ether on those with and without goitre. This was brought forcibly to me after the loss of some cretin dogs by attempting ether anæsthesia. On inquiring into the matter I found that it was common knowledge about the laboratory. The janitor was aware of the danger of sudden death and avoided goitrous dogs for use in the physiological department. In Dr. Crile's work great differences in resistance were noticeable and as I examined all the thyroids in routine, I could sort out those dogs with excellent resistance by their more normal thyroids.

Dr. D. H. Dolley, in his large experience with dogs in Crile's laboratory also noticed great variations in their resistance to ether and he told me that he avoided using goitrous dogs when possible.

That there are great variations in the resistance of dogs to ether is clear and it occurs for the most part in those with hyperplasia of the thyroid and enlargement of the lymphoid tissues.

The question arises: Have these changes any causal relation to the phenomena of lowered resistance and sudden death? I think there is a definite relationship for the following reasons:

(1) It is limited to those dogs and sheep which have goitre and general prominence of the lymphoid tissues.

(2) Administration of iodine will relieve the danger.

(3) Toxic (exophthalmic) goitre in man, having practically the same anatomical changes, show the same phenomena of lowered resistance and danger of sudden death under ether anæsthesia. Extensive data are not yet in hand, but an hypothesis based on our observations thus far may not be misleading. That is these subjects may be suffering from an exhaustion which particularly manifests itself in the central nervous system, and that this exhaustion with its consequent dangers is comparable to that occurring in severe anæmias; in the one case there is an iodine deficiency, in the other it is iron.

(4) *Effect of iodine on the human thyroid.*—I have but one observation namely: That of 173 human autopsy specimens examined, all of those cases which had had iodine administered just prior to death showed the acinar epithelium to be in the quiescent (low cubical) stage.

Complications in the Dogs' Thyroid.

They are rare. Hæmorrhagic-cystic (28) changes are the usual ones. They generally occur during the stage of glandular hyperplasia. They seem to depend on an insufficient stroma reaction to support the great increase in the blood-supply and epithelial elements with consequent rupture of the smaller vessels. In colloid goitres, calcification, though very rare, is the most common, and usually occurs in the walls of the arteries and the capsule of the gland.

Conclusions.

(1) That iodine is essential for normal thyroid activity.

(2) That glandular hyperplasia is a physiological reaction to a deficiency, and it is to be considered cretinoid in nature.

(3) That colloid goitre is usually preceded by a stage of glandular hyperplasia, and in its uncomplicated form is the quiescent stage of the same.

(4) That the associated enlargement of the spleen, thymus and lymph glands, in varying degrees, is an integral part of the affection.

(5) That the dangers associated with ether anæsthesia in dogs are similar to those observed in toxic (exophthalmic) goitre and lymphatism in man.

(6) That the commercial desiccated thyroid contains a mixture of normal and abnormal thyroids, and that this explains a part of its varied action clinically.

(7) That further observations will show a closer relationship between the glandular hyperplasias in animals and toxic (exophthalmic) goitre in man than has been indicated.

I wish to thank Dr. R. G. Perkins for help with the microphotographs, and also Drs. M. B. Bonta and C. H. Lenhart for their unstinted services in the operative work.

Literature.

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Notes on the Microphotographs.

The sections were taken from the routine files and represent types and moderate degrees of the changes. All sections are formalin (four per cent), celloidin-hæmatoxylin, and eosin preparations unless otherwise indicated. The magnification is the same in all. Leitz, oc. 4, obj. 3, × 95 diameters.

(1) Normal human thyroid (Zenker spec.).

(2) Primary toxic (exophthalmic) goitre, human (Zenker spec.).

(3) Colloid goitre, human.

(4) Normal thyroid, dog.

(5) Moderate glandular hyperplasia, dog.

(6) Early stage of colloid goitre, dog (reversion of early stage of glandular hyperplasia). Note the remnants of intra-acinar projections; also compare with the normal.

(7) Normal thyroid, sheep.

(8) Moderate grandular hyperplasia, sheep.

(9) Colloid goitre, sheep.

(10) Normal thyroid, ox.

(11) Moderate glandular hyperplasia, ox.

(12) Marked glandular hyperplasia, ox.

(13) Moderate glandular hyperplasia, dog. (Specimen removed before the administration of iodine.)

(14) Same gland as No. 13. (Specimen removed during the administration of iodine.)

(15) Same gland as No. 13. (Specimen removed after the administration of iodine.)

(16) Composite picture showing moderate glandular hyperplasia of right lobe, and reverted (colloid) stage of left lobe. The left lobe was removed four weeks after the right, and iodine was administered in the interval.

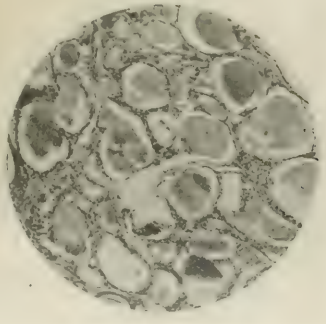

FIG. 1

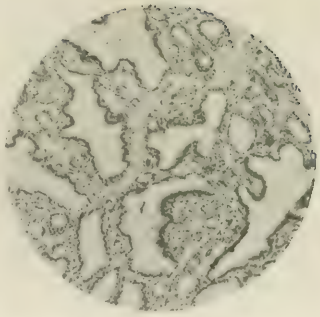

FIG. 2.

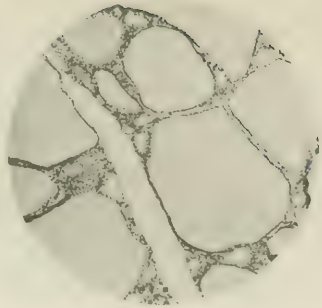

FIG. 3.

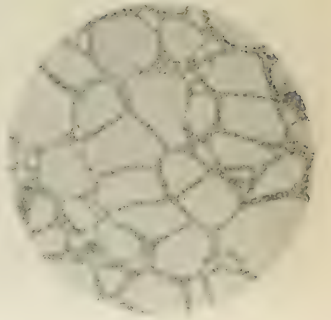

FIG. 4

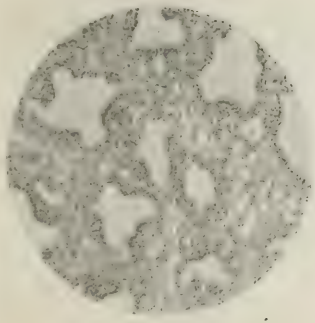

FIG. 5.

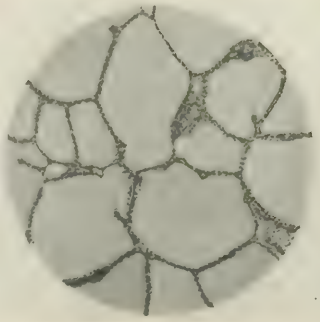

FIG. 6.

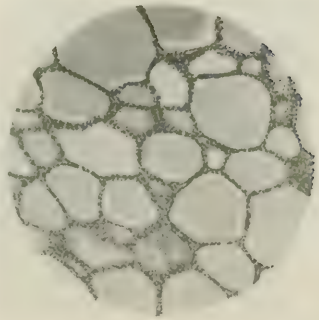

FIG. 7.

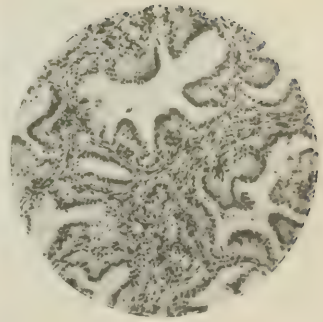

FIG. 8.

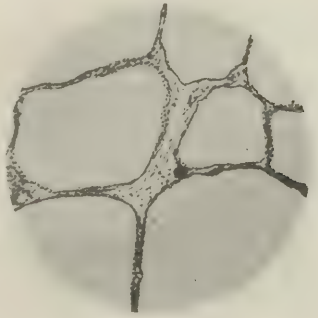

FIG. 9.

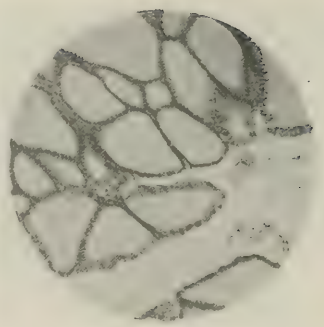

FIG. 10.

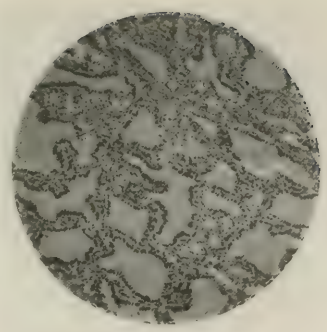

FIG. 11.

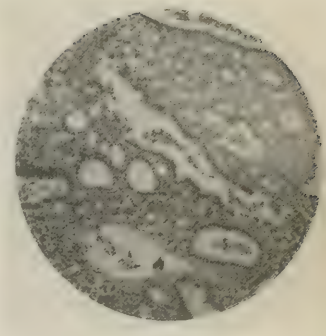

FIG. 12.

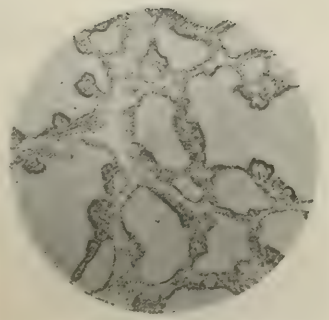

FIG. 13.

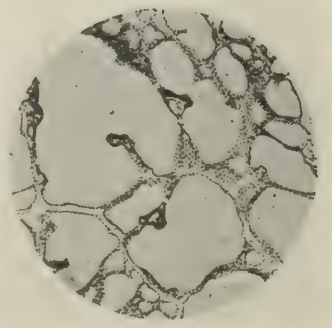

FIG. 14.

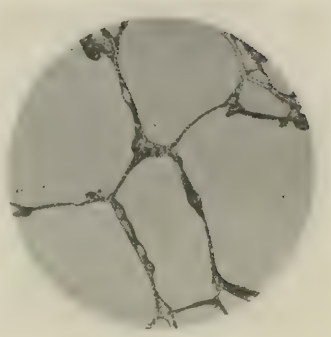

FIG. 15.

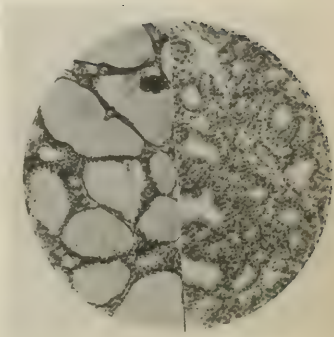

FIG. 16.

EXPERIMENTAL EPITHELIAL PROLIFERATIONS OF SKIN AND MUCOUS MEMBRANES.

By Henry F. Helmholz, M. D.,
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The work of Fischer has opened up an entirely new line of experimentation regarding the development of tumors, and it was with the idea of repeating his experiments and carrying the work a little farther that this work was undertaken. The very first experiment proved quite conclusively (Fig. 1), that epithelial proliferation of the skin could be readily produced by the injection of a solution, Sudan III, in oil, and sections were obtained that resembled epithelioma of the skin in no slight degree. The negative results of Fischer in the breast, stomach, and intestines were at first substantiated by the results obtained in several operations and injections in the stomach. The abruptness with which the connective tissue changes stopped at the muscularis mucosa made it seem that perhaps the technique was at fault and the oil had no chance to act on the epithelium; so the experiments were repeated on the rectum, where the injections could be made as frequently as necessary, and the oil more readily inserted into the mucosa. The mucous membrane of the mouth also proved to be a very fertile field for experimentation.

In the following paragraphs, the various experiments performed will be briefly given.

The work on the skin was performed on the rabbit, guinea-pig, and chicken. The experiments on the rabbit's ear covered the greater part of the work. The first one was the repetition of Fischer's experiment, and as the photo-micrographs are given in the text, the details will be briefly indicated.

Exp. I*a*.—Large black rabbit.

January 16, 1907, 11 a. m. Injected Sudan III oil into the middle of the lateral margin of both ears.

January 18 and 22. Repeated the injection. The left ear is only slightly thickened and the skin shows slight, if any, excoriation. The right is greatly thickened and excoriated over its entire surface; it is about three times its normal thickness.

January 28. Pieces removed from both ears.

February 1. Animal died. Blocks taken from both ears. Autopsy showed nothing of note except that glands at the base of ears are large, swollen, and distended with oil. Considerable oil in capillaries of lungs.

In the gross, the excised portions had very much the appearance of the cut section of a carcinoma of the skin, small finger like processes of a slightly more opaque white color could be seen extending down into the fibrous tissue. This was even better brought out after the piece had been hardened in alcohol and all the Sudan oil dissolved out.

Microscopically, the section is one of the most interesting of the series (Fig. 2). The injected side of the ear is about three times the size of the inner which has been only affected by the oil that has passed through the fenestra in the cartilage. The surface epithelium is greatly thickened, which is due in part to an increase in cells and in part to small vesicles which contain serum and a few pus cells. The cells of the epidermis, although they are rapidly proliferating as shown by numerous mitotic figures, do not extend any great distance downward into the fibrous tissue. The greater part of the epithelial proliferation comes from the hair follicles and sebaceous glands which have grown to such a degree that they cannot be distinguished, only the large concentrically arranged epithelial masses of chitinous material indicating the original follicles. Contrary to the assertion of Jores, it seems quite evident that the most marked downward growth is from the lower portions of the hair follicles; connections can be traced from them down almost to the cartilage. At the level of the hair follicles, the masses of epithelium take up the greater part of the surface, but lower down the ear consists of a mass of young fibrous tissue in which lie very numerous small masses of epithelium in bizarre shapes, and when growing around oil droplets, they form a thin lining of slender cells that are drawn out like fibroblasts. In the large masses there is considerable central epithelial degeneration, resembling somewhat the pearls of carcinoma. The mitoses are very frequent, but contrary to Fischer's findings, are nearly all regular.

On the opposite side of the cartilage, the picture is that of the reaction when the irritant is less intense, showing merely the thickening of the epidermis, and the rapid proliferation of the cells of the hair follicles and glands, without any marked downgrowth of epithelium into the deeper tissues.

The sections taken on the 16th day are of interest because they show the very rapid degeneration of the epithelium. Almost the entire mass of cells excepting perhaps the outside layer in contact with the stroma show marked degenerative changes; the nuclei are dark and shrunken, the cell outlines indistinct and the protoplasm filled with bluish grandular material. Mitotic figures are absent.

The other six experiments with Sudan III, and Scharlach R oil gave practically the same results except that the epithelium did not show quite so much splitting up into small masses. One of the experiments showed very beautifully the invasion of the cartilage by the epithelium; as already previously described by Fischer. The perichondrium and a small portion of the cartilage has been destroyed and a number of cartilage cells have become necrotic.

In the course of his discussion, Fischer makes the statement that if the chemotatic action of the oil could be made a continuous one, the growth of the tumor would be constant and malignant. Working along this line, two rabbits were injected once a week for a period covering two months.

The reaction was very nearly the same in both animals, the ears gradually increased in size, became very firm and elastic, and the surface formed at first thick scales and later cast off large masses of white epithelial debris. At this stage, the

injections became very difficult to make because of the large epithelial pearls that rapidly ruptured as soon as the oil was forced into them. Portions of the ear were removed 34 days in one and 52 days in the other after the first injection of Sudan III oil. In the gross, the one specimen was a greatly thickened ear tip measuring 5-6 mm. across in its widest portion; as the two were practically identical as far as the epithelial changes go, the one in which a chondroma was produced will be briefly described. The surface was quite rough and irregular, and with the finger, several large white masses which projected above the surface could be shelled out. The same structures were found deeper down in the fibrous tissue on the cut section and could be readily expressed on pressure. The fibrous tissue contained considerable pigmented oil, but none was seen in the epithelial spaces.

Microscopically, the thickening is seen to be due to great proliferation of fibrous tissue which, especially in its outer portion where it comes in contact with the epithelium is of a very loose texture, being formed almost entirely of spindle cells. In its central portion, there are numerous, good sized vacuoles, some without a lining which no doubt in the fresh state contained oil, and others filled up with a rather irregular mass of cells, the outlines of which are indistinct; their nuclei, however, are large and vesicular.

The most marked feature of the epithelial proliferation are the large cysts lined by a thick layer of proliferating epithelium, in which a small number of mitotic figures can be found. Some of the cysts open on the surface, others are deeper down and completely surrounded by fibrous tissue. The surface epithelium is for the most part a thin layer of cells that sends occasional processes into the loose tissue beneath. At one end of the section between two diverging plates of cartilage there is a multiple chondroma developing in the loose fibrous tissue. These plates show some lateral outgrowth of cartilage. The areas of cartilage vary from masses about 1 mm. in diameter to minute ones consisting of only four or five cells. These cartilage cells can be seen in all transition stages from connective tissue cells.

The organs at autopsy showed nothing of note except the marked sclerosis of the gland draining the ear. Nothing comparable to the proliferation of the alveolar epithelium as described by Fischer could be demonstrated in numerous sections of the lungs.

To determine what part, if any, the oil played in the process, various other solvents were substituted for the oil. Paraffin (melting pt. 45°) was tried, but it was found that although the epithelial changes were produced to a slight degree, the material had a great tendency to collect in such large masses that it produced necroses. A mixture of oil and paraffin was next tried with better success, and although the combination does not produce the pretty results that the oil alone does in the skin, it was found to be of great value in the experiments in the mucous membranes, where oil alone is too rapidly absorbed.

The specimens produced by Sudan oil-paraffin showed a great tendency on the part of the fibrous tissue to form large conglomerate masses of giant cells. The epithelium in 15 days had grown quite diffusely down into the newly formed tissue, on a small scale to be compared with Fig. 1.

Sudan III dissolved in ether, xylol, and dilute alcohol all produced such acute irritation that they led to necrosis on repeated injections.

Two experiments tried with osmic acid oil, and two with dimethylamidoazo-benzol (the latter a product related to Sudan III, but of basic instead of acid properties) were negative. There was some thickening of the epithelium and even some proliferation of the cells of the hair follicles in a 19-day dimethylamidoazo-benzol specimen. The osmic acid experiments were very nearly the same. A specimen obtained after 4 injections covering a period of 17 days, showed some slight thickening, and in several small areas a hyperplasia of the hair follicle cells but not to be compared with a Sudan specimen of the same age.

The four experiments on guinea-pigs with Sudan oil and Sudan oil-paraffin gave the same results as in the rabbit. A 15-day specimen of the oil injection shows a very marked thickening of the surface epithelium and in the lower layers, numerous mitotic figures can be seen, especially in those areas where epithelial processes are extending down into the very cellular fibrous tissue. The hair follicles also show very marked increase in size and from their lower portions numerous processes extend out irregularly into the inflammatory tissue. The addition of paraffin changes the microscopic picture considerably. The reaction is more local, the side opposite is not affected at all and the injected side only a very short distance laterally. The ear is considerably thicker than the other, due principally to a great increase in fibrous tissue in which foreign body giant cells are a very marked feature. The epithelium is markedly thickened and has grown completely around the great mass of oil-paraffin. From its under surface, small epithelial buds extend into the fibrous tissue. To the side of this central mass, the proliferation of the hair follicles is quite marked. Mitotic figures are very frequent.

The only other animal that the injection of Sudan oil was tried on was the chicken. The comb and the skin under the wing were injected, the latter with oil-paraffin. The results were negative; there was produced a considerable thickening of the epithelium but no downgrowth in either place. That the oil came in direct contact with the epithelium is shown by the formation of young connective tissue just beneath the epidermis.

Having determined that the Sudan oil acts with great constancy in producing epithelial proliferations of the skin, its effect was next tried on the various mucous membranes of the rabbit. The lining of the bladder, œsophagus, stomach, rectum, and mouth were injected with a mixture of oil and paraffin in the majority of cases.

1. *Bladder.*—A laparotomy was performed and the Sudan oil-paraffin injected by inserting the needle through the serosa of the bladder. Two rabbits were injected; one was sacrificed 12 days after the operation and the other after 22 days. In the second, a small area was injected with dimethylamidoazo-

benzol oil. Microscopically, the bladder on opening presented a large papilloma distended with oil. On microscopical examination, there was found a great growth of fibrous tissue just under the epithelium but no proliferation whatever of this tissue. The same condition was found in the dimethylamidoazo-benzol injections.

2. *Œsophagus.*—An incision was made into the neck of the rabbit, the œsophagus was dissected out, and injected with oil at one point, and 2 cm. lower down with oil-paraffin. The animal was sacrificed 12 days later. The findings consisted of a marked proliferation of fibrous tissue, rich in giant cells in the submucosa. Epithelial changes were entirely absent.

3. *Stomach.*—The two attempts to produce proliferation of the gastric mucosa failed. The abdominal cavity was opened, the muscle coats cut through and the Sudan oil-paraffin injected directly into the submucosa. In each case, there was a marked fibrous tissue reaction in the submucosa which extended as far inward as the muscularis mucosa and then ended abruptly, the mucosa being perfectly normal.

4. *Mouth.*—The relation of the epithelium of the mouth and skin is so close that it was almost to be expected that the epithelium of the former would react to Sudan III like the latter, and so it proved to be. Six experiments were performed, three with Sudan oil and three with Scharlach R oil-paraffin.

Exp. II*a*.—White and gray rabbit.
February 4, 1907. Injected Soudan III oil into right cheek.
February 11. Repeated injection.
February 15. Repeated injection.
February 18. Repeated injection.
February 21. Excised injected portion of cheek under ether.

The section shown in Fig. 3 was taken from this block and shows very well the character of the epithelial downgrowth, a slender process that spreads out and grows around the mass of pus cells that have collected in the oil droplets. The mitoses are very numerous.

In another section, removed six days after a single injection with Scharlach R oil-paraffin, only thickening of the surface epithelium and numerous mitotic figures in the basal layer of cells are to be made out.

The most diffuse growth of epithelium in the tissue was obtained in Exp. II*f* after three injections of Scharlach R oil-paraffin in the cheek. The section is shown in Fig. 4. The epithelium is growing in great masses diffusely in the tissues, surrounding masses of purulent exudate, and extending out in thin streaks to oil drops further along, surrounding them and penetrating still further into the new formed fibrous tissue. This same rabbit had five injections of Sudan oil-paraffin into another portion of the mucous membrane, and was finally sacrificed on the 34th day after the first injection. In the gross, the downgrowth of epithelium could be made out as several grayish lines extending in from the surface; although the epithelium is in larger masses, it does not show nearly the diffuseness of growth of Fig. 4. Throughout the infiltrated portion, there are numerous polymorphonuclear leucocytes. In these large epithelial masses, the preservation of the cells is much better than in those of the same size in the skin.

5. *Rectum.*—The failure of the experiments in the stomach and œsophagus seemed to be attributable to the presence of the muscularis mucosa which prevented the necessary direct action of the oil on the epithelium. To overcome this obstacle and also to make more frequent injections possible, the rectum was selected to work on. The technique employed was simple. The rectum was stripped back until a large portion of mucosa was visible. The needle was then introduced, either through the mucosa, or inserted in the skin just beyond and carried out under the mucosa. Multiple injections were made each time, as it was very difficult to get the oil in just beneath the mucosa. The first two experiments were negative. In the first, three injections of Sudan oil were made, the animal dying on the 12th day, and in the second, the animal died on the 22d day after three injections. Except for slight fibrous tissue changes in the submucosa, there was no difference from the normal. The third experiment because of its importance will be reported in detail.

Exp. VIII*b*. Large gray and white female rabbit.
February 28, 1907. Injected Scharlach R oil-paraffin under rectal mucosa.
March 5. Repeated injection—small amount.
March 7. Repeated injection—small amount multiple.
March 12. Repeated injection.
April 4. Repeated injection.
April 23. Repeated injection.
April 30. Repeated injection—large amount retained.
May 9. Repeated injection—large amount retained.
May 14. Repeated injection.
May 17. Animal died without any apparent cause.

The organs were found practically normal.

Gross description of the rectum: On opening the rectum a considerable amount of oil oozed from the section. The submucosa was greatly thickened by fibrous tissue and oil droplets. At one point, just inside the line of juncture of skin and mucous membrane, there is a small white nodule lying just below the mucosa. Making several other longitudinal cuts, two other areas of similar nature are found. In the one, there are several grayish white lines extending for some distance down into the submucosa; in the other, there is a larger grayish mass lying in the submucosa. A diagnosis of probable downgrowth of epithelium was made.

Microscopically, this diagnosis was verified. There has been produced multiple downgrowth of cylindrical epithelium into the submucosa. In two of the sections, the connection with the mucosa cannot be made out. The alveoli are more or less normal, although in both there is one large irregular lined space. In both, there is some increase of fibrous tissue in the mucosa and numerous vacuoles formed by oil droplets, but no definite metaplasia of the epithelium.

The third section from which Fig. 1 is taken is markedly different; the proliferation is more irregular and there has been a metaplasia of cylindrical to squamous with a return to

the cylindrical type in some of the alveoli further down in the tissue. The section was cut parallel to the rectum so that there is no possibility that the squamous epithelium, found, as it is, with the cylindrical epithelium on both sides of it, got there by the obliquity of the cut. In the part from which the downgrowth has taken place the epithelium shows great thickening, the single row of cylindrical cells shades over into a layer of squamous epithelium varying from five to ten cells in thickness; at the base of several of the processes, the cells on the surface return to the cylindrical form. The squamous epithelium above narrows down to a several cell layer and gradually changes back to the cylindrical type. The epithelium rests on a newly formed connective tissue rich in plasma cells and containing some eosinophiles and oil vacuoles.

The muscularis mucosa has been broken through and pushed to the side by the large epithelial masses.

Beneath the muscularis mucosa, the other main solid epithelial mass of squamous epithelium opens up into a large space partly filled with detritus and lined by many layers of squamous epithelium which on the surface has a marked tendency to return to the cylindrical type. Extending out from this alveolus, are numerous small solid processes which in cross section show a tendency to the formation of alveoli, and the lining cells a return to their original form. A single alveolus lined by three layers of cells, the inner most one of which is cylindrical, is found down in the inner muscular coat; its connection with the main mass of epithelium could not be made out in any of the sections. At one other point just beneath the muscularis mucosa there is an alveolus filled with detritus in which are seen numerous leucocytes and lined by a single layer of cuboidal cells. Some mitoses are found but only infrequently.

The positive results obtained in this last experiment make it seem probable that with improved technique, the same sort of changes can be produced in stomach and œsophagus.

The experiments show quite conclusively that the effect of Sudan III and Scharlach R is a general one, that they act on different sorts of epithelium as well as on the different connective tissue elements including cartilage.

The fact that he could obtain proliferation only of the skin has led Fischer to suppose that Sudan III and Scharlach R had some definite chemical affinity for the surface epithelium. That there is some interaction cannot be doubted after examining Fischer's illustration, but that this action is in any way specific, the above given experiments controvert quite definitely and no doubt, if the experiment that was performed in the rectum were repeated in the stomach, intestines, and œsophagus, identical results would be obtained so that the action of the Sudan III can hardly be thought of as a specific attraxin, but rather something that by interaction with the connective tissue produces a soil that is ready for epithelial development. The development of cartilage from fibrous tissue seems more evidence to show how marked is the effect of the Sudan oil on the connective tissue.

In the skin experiments, Jores reports most of the epithelial growth from the hair follicles at the entrance of the sebaceous glands, and thinks that failure on mucous membrane may easily be due to absence of hair follicles. In cases where the reaction is very mild it does seem as though most of the effect manifested itself in the upper portion of the hair follicles but whenever any more active proliferation occurs, the skin and especially the lower portions of the hair follicles respond to the attraxin. As regards mucous membranes, the numerous positive results in mouth and rectum indicate the relative importance that the hair follicles play. The work of Snow is rather difficult to explain; how he could have obtained such a series of absolutely negative experiments is hard to see when in practically every experiment on the skin more or less marked proliferations of the skin were obtained. His conclusions are hardly justifiable, especially as it is almost inconceivable that Fischer's results and drawing could be due to any obliquity of the section. The work of McConnell, Jores, and that just described, all confirm the essentials of Fischer's work.

The experiments on the rectum are perhaps of more interest than any of the others. It proves that very close contact must take place between epithelium and oil in order that any reaction take place; and it explains the negative results obtained in the stomach and œsophagus, though not of the bladder. It further shows that cylindrical epithelium remains so, only so long as it lines a lumen, and as soon as it grows in masses it conforms to the squamous type; and just as readily returns to the cylindrical type when lumina form in the epithelial masses. The same thing occurs in the intestinal tube during embryonic development. The canal becomes obliterated by an excessive proliferation of epithelium which is of the squamous type, and as soon as small lumina again appear the cells about them return to their cylindrical form. This metaplasia, though of great interest, shows how different the process is from carcinoma in which the character of the cells remains constant.

The relation of these experiments to the cancer problem has been dealt with at great length by Fischer, who has set up an entirely new theory to explain the growth of malignant tumors. The quite uniform action of Sudan on the different epithelia makes it seem that it is rather a common reaction on the part of epithelium than a specific attraxin that produces the very interesting proliferations. The importance of Fischer's work is quite manifest, and will lead without doubt to many interesting and useful results.

In conclusion, I desire to thank Dr. Welch for his kind suggestions and the interest that he took in this work.

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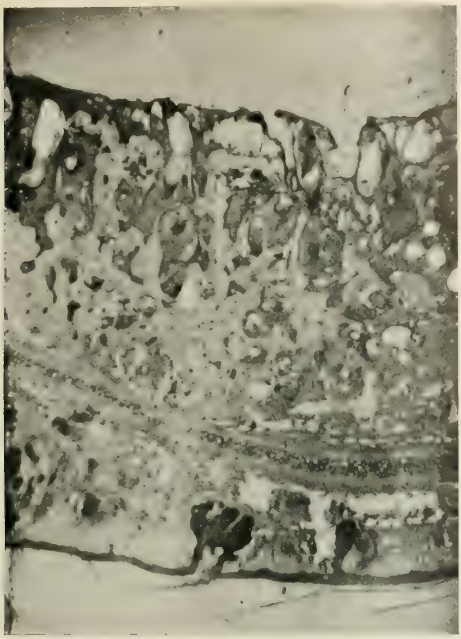


FIG. 1.—Experiment Ia. Showing gross relations of epithelial processes growing down into tissue of ear. 12-day specimen.

FIG. 3.—Experiment IIa. Mucous membrane of mouth. 17-day specimen.

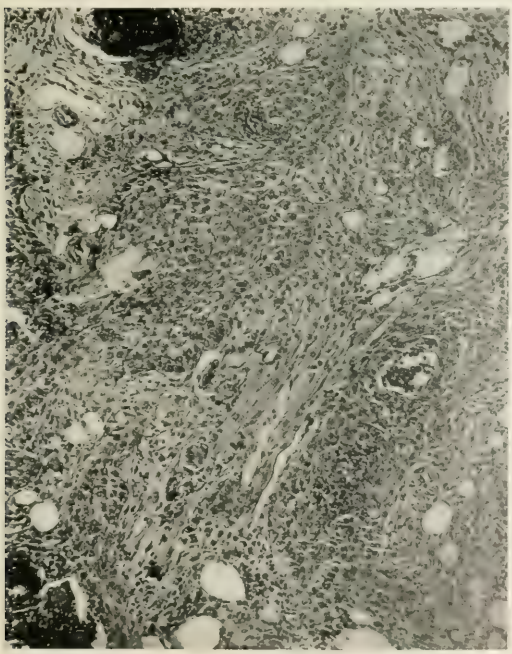


FIG. 4.—Experiment IIb. Mucous membrane of mouth. Growth of epithelium deep in tissues.

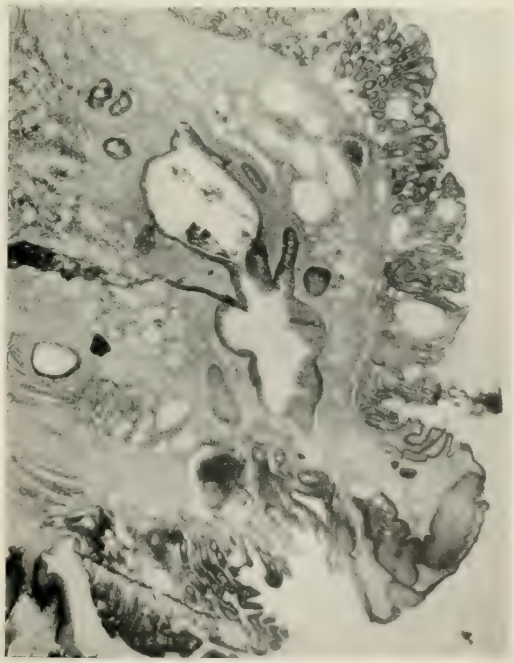


FIG. 5.—Experiment VIIIb. Rectum. Metaplasia and downgrowth of cylindrical epithelium.

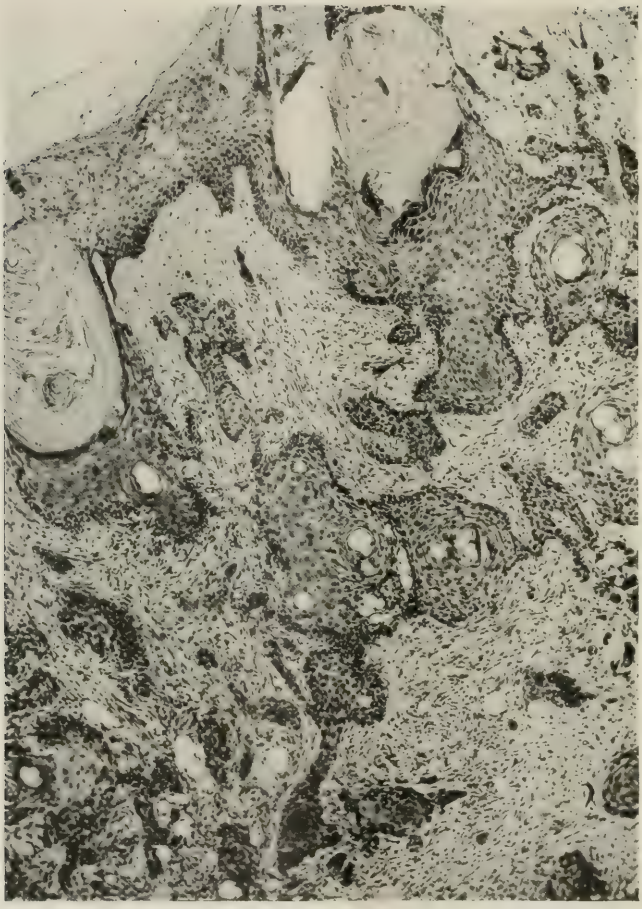


FIG. 2.—Experiment Ia. Showing proliferation of epithelium of rabbit's ear in detail. 12-day specimen.

AN EXPERIMENTAL MULTIPLE CHONDROMA.

By Henry F. Helmholz, M. D.,
Fellow in Pathology, Johns Hopkins University.

In the course of experimentation in rabbits to determine what effect the oft-repeated and long-continued injections of Sudan III oil would have on the epithelium of the rabbit's ear, there was found on microscopic examination of a block of tissue, removed a little over two months after the first injection, a multiple chondroma. At the time only a small portion of the ear was removed and the injections continued. The animal died suddenly a month and a half later, and when picked up in the morning it was noticed that the injected ear had been entirely eaten away, and the further development of the tumor unfortunately lost. The length of time necessary for the experiment prevented a repetition of the same. Another animal that had been injected for a period of about one month and a half showed no cartilaginous changes. In several others, however, of somewhat shorter duration, small outgrowths from the sides of the cartilage plates were noted, but in none, were any distinct masses of cartilage lying free in fibrous tissue.

The technique employed in the experiment is in brief as follows. A solution of Sudan III (Grübler) in olive oil, containing an excess of the pigment was prepared and sterilized and, while still hot, injected with a sterile hypodermic needle as near as possible into the tissue just beneath the epidermis. From five to ten minims were injected, but rarely more than half of that amount remained within the tissue. While making the injection the ear was clamped just below the point at which the needle was inserted so that as little as possible of the oil passed immediately into the circulation. This may account for the long life of the rabbit.

The following is a brief outline of the experiment:

Exp. Ie.—Large white rabbit, female.

January 31, 1907. Sudan III oil injected into both ear tips.

February 4. Tip of left ear removed. Right slightly swollen.

February 11. Right ear re-injected. Ear greatly swollen, tender and scaly.

February 13. Right ear re-injected. Ear greatly swollen, tender and scaly.

February 18. Right ear re-injected, only small amount of oil retained.

February 21. Right ear re-injected, ear markedly swollen, thick scales on, in, and outside of ear. Swelling limited entirely to tip.

February 28. Right ear re-injected. Swelling has subsided to some extent. Ear thick and elastic.

March 8. Right ear re-injected. Rather difficult to inject oil because of numerous large spaces filled with epithelial debris which quickly ruptures when the oil is forced into them.

March 14. Right ear re-injected. Numerous large degenerated epithelial masses can be scraped out of the surface.

March 20. Right ear re-injected.

March 27. Right ear re-injected.

April 4. Removed small portion of ear tip.

The tip of the ear measured 6 mm. in thickness on cross section. Its surface was rough and irregular, from the depressions small masses of putty-like material could be scraped. The cut section showed an ear thickened out of all proportion by an increase in fibrous tissue, in which numerous large epithelial alveoli filled with debris could be seen; this material was readily squeezed out. In the fresh state there was considerable oil in the stroma, but none in the epithelial masses. No evidence of cartilaginous proliferation was made out in the gross.

On microscopic examination there was found at one end of the section a mass of very loose fibrous tissue, in which numerous large and smaller islands of cartilage were developing. A single cartilage plate extended almost the entire length of the section. Just before reaching this area it divided into two plates which diverged at an angle of about 45°.

It might be supposed that the cartilage plate had here been torn apart, but comparing the position of the plates in a number of sections and the presence of a V-shaped mass of cartilage at the apex of the triangle, made it certain that there were normally two plates of cartilage. Along their surfaces there were numerous small knob-like thickenings, consisting of young cartilage cells. The angle formed by these two sheets of cartilage was filled in with a loose newly formed fibrous tissue, containing numerous large vacuoles, which no doubt in the fresh state were filled with oil. In the inner portion of the angle the fibrous tissue is somewhat denser and more vascular, and showed several alveoli filled with proliferating endothelium. Farther out the predominent cell is a small stellate one, bound together by a thin network of fibrils; in areas these cells become grouped together in bundles. The large vacuoles, made by the oil were in part lined directly by the masses of cartilage, in one instance completely as seen in Fig. 1. It is in this loose tissue that the numerous masses of cartilage were found. The connective tissue shaded off so gradually into the cartilage, that at many points it was difficult to determine where one began, and the other left off. This was especially true of several of the more centrally lying masses that were not surrounded by perichondrium, in which the connective tissue cells could be seen in all transitions to cartilage. Fig. 2 shows the condition extremely well. The cartilage, as seen in Fig. 1, was present in large masses which stained typically blue, and in small areas, some of which consisted of only three or four cells. In the latter the cartilage cells could be seen lying free in a uniform pink staining hyaline mass, in which occasionally fibres could still be made out. In several of the larger areas of cartilage the cells had undergone necrosis, and the cell spaces were filled with blue granular detritus, in others as many as five cells could be found in a single lacuna; in still other areas, especially the younger ones, multinucleated cells were found, but in no instance were any karyokinetic figures definitely made out, although many structures were seen that resembled them.

In these same small masses the cells have undergone vacuolar degeneration, and what was more remarkable the nuclei of many have increased so in size that they fill practically the entire lacuna.

The areas of especial interest were those in which the cells were in transition stages to cartilage. The connective tissue cells seemed to draw in their processes, and their outline became very distinct, and their nuclei became larger and more vesicular. The interstitial substance lost its fibrillar character, and stained lighter and more uniformally pink, and the cell body, which at first was still directly in contact with it, retracted and was seen to lie free in its lacuna. So that just before the cell retracted it is impossible to say whether it was a fibroblast or a cartilage cell that one was dealing with.

This experiment showed that Sudan III, besides its decided effect on epithelium also exerted a powerful stimulating influence upon the cartilage producing tissues. The direct proliferation of the cartilage cells was seen by the thickening of the primary cartilaginous plates; the growth of the independent islands of cartilage, however, could not be so explained. The direct transitions from connective tissue to cartilage showed that in great part the masses were produced by metaplasia. Two explanations are possible: (1) That the perichondrium of the normal plates has undergone enormous hyperplasia, and, in its rapid growth has produced a tissue of very loose fibrillar type which is again slowly assuming its cartilage forming function; or (2) That the connective tissue by the stimulation of the Sudan III has returned to the type of embryonic mesoblastic cell, with the power of forming any of the connective tissue elements. It might be supposed that the original cartilage plate had been broken into small fragments by the pressure of the injections, but that seems rather improbable, and would not explain the metaplasia.

Of the two theories proposed it seems that the first has the most in its favor. The Sudan oil has produced a marked proliferation of perichondrial cells, just as it acts on the other connective tissue cells. This growth has been so rapid that for the most part the cells have retained their embryonic form of stellate cells, and only later as they slowly ripen begun to change into cartilage cells and these in turn gone on proliferating to form the large masses, as seen in Fig. 1. It seems more rational to think of the process rather as an excessive stimulation of perichondrial cells, than the taking on of a new function by the ordinary connective tissue cell. Microscopically, the stellate cells that were developing cartilage cannot be distinguished from another connective tissue cell of the same type.

The bearing that this experiment has on the views of Fischer regarding the specificity of action of Sudan III, might be dwelt on for a moment. In his article he described the action of Sudan III as specific for the epithelium of the skin; that a definite attraxin produced the proliferations; that attraxin is not specific for squamous epithelium was shown in another place (2), and this experiment shows that a specific connective tissue element cartilage responds to the same attraxin, so that if the action is to be considered as due to an attraxin, its nature and action must be far more general than Fischer described.

At this point I wish to thank Dr. Welch for the kind interest he has taken in this work.

As far as can be determined from the catalogue of the Surgeon-General Library and the Index Medicus this is the first time that a chondroma has been experimentally produced.

TWO CASES OF ATRESIA OF THE SMALL INTESTINE.

I. MULTIPLE CONGENITAL ATRESIA OF THE JEJUNUM.

II. VALVULAR ATRESIA AND SECONDARY INFLAMMATORY OBSTRUCTION OF JEJUNUM.

By Henry F. Helmholz, M. D.,
Fellow in Pathology, Johns Hopkins University.

Atresia of the small intestine is a condition that is still very unsatisfactorily explained in the great majority of reported cases. One thing which has been quite consistently neglected is the histological examination of the specimens. How this may affect the etiology is best illustrated by Case III of Chiari's series in which, on macroscopic examination, he came to the conclusion that the occlusion was due to axial twisting of the mesentery, but after making microscopic preparations, he discovered an intussusceptum in the distal loop, and so decided that the primary cause was the intussusception. The two cases named in the title become of especial interest when viewed in the light of the histological findings. The cases in detail are as follows:

Case I.—Baby S. Aet. 2 days. Died October 21, 1906.

Clinical History.—Family history was negative. Child was born in cab on way to hospital. On arriving in ward child cried and breathed well, its head and arms were markedly cyanotic. It was a typical blue baby, a systolic murmur was heard loudest over sternum and present also over entire chest. The child did not vomit. It was given hot water and brandy in small amounts and strychnia. Its weight at birth was 2755 gm., on the second day, 2568 gm. Temperature, 95°. Death occurred on second day. The autopsy, 2800 of the Johns Hopkins Hospital series, showed the following conditions:

Anatomical diagnosis.—Malformation of heart; congestion of viscera and subcutaneous tissue; multiple congenital atresia of intestine; broncho-pneumonia; uric acid infarcts of kidney; cirrhosis of liver; chronic fibrous peritonitis; cirrhosis of pancreas; anomalous mesenteric circulation.

Body was that of a white male child of good development; 50 cm. in length. Rigor mortis had set in. The face and neck were of a deep purplish color, and the entire trunk and extremities had a pale bluish tint. There was moderate development of the subcutaneous fat. On opening the peritoneal cavity it was filled principally by several large distended loops of greenish congested

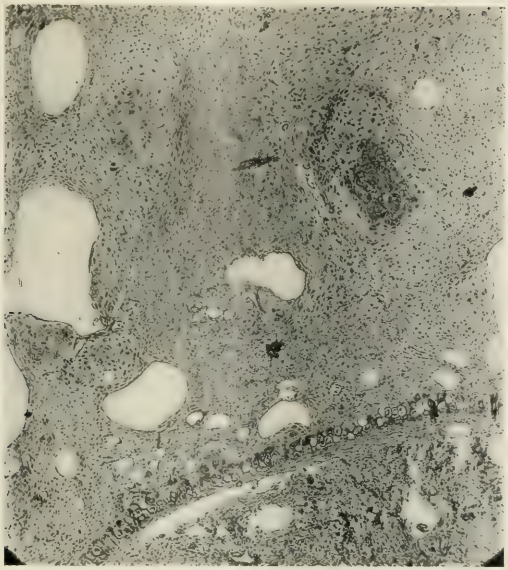


FIG. 1.—Multiple areas of cartilage and oil spaces.

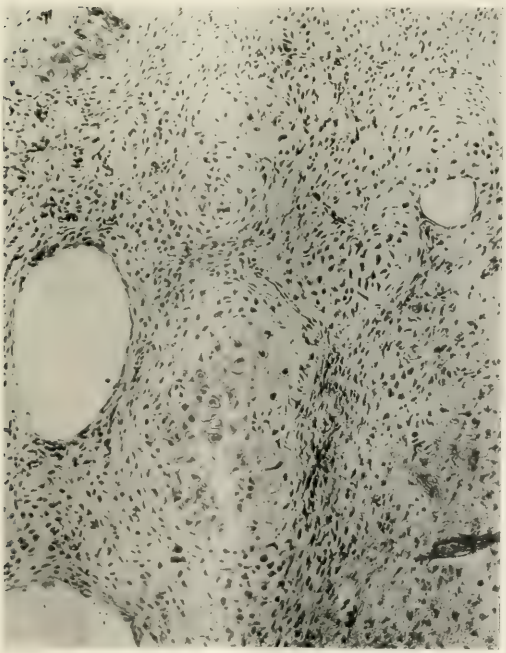


FIG. 2.—Transition of connective tissue cells to cartilage.

bowel. The cæcum was situated in about the mid-line, held loosely by a well developed mesentery. The appendix was normal except for position. In the left lower quadrant lay several coils of very nearly normal appearing intestine. The stomach was normal, but the duodenum, jejunum and a part of the ileum were enormously distended. This distention ended suddenly in a blind sac, from which extended several centimeters of obliterated bowel. The intestinal coils were bound together by fine fibrous adhesions. The pleural and pericardial cavities were normal.

Heart showed transposition, the apex being directed toward the right. On the outside no line of division can be seen between the ventricles. On opening the heart, both auricles were found to form a single cavity, as did also the ventricles.

Lungs were deeply congested. On section the anterior portions were of a pinkish red color, the posterior of a deep purple.

Kidneys were of normal size, showing well marked fœtal lobulations. The opaque gray cortex measures 2 mm. across. Running down the pyramids were orange yellow linear streaks.

Organs of neck.—The trachea and œsophagus were normal. The thyroid was large and nodular, and showed on section an increase in fibrous tissue.

Brain was negative.

Liver was slightly enlarged, measuring 9½ x 6 x 3 cm. Its surface was everywhere smooth and glistening, except where the duodenum was adherent to it. The organ was of a reddish brown color and of normal consistency. Running over the entire surface was seen a fine tracery of grayish lines. On section the parenchyma was of a yellowish red color, the center of the lobules having a slightly redder, the periphery a slightly more yellowish tint. About the lobules could be seen the same fine gray lines that were seen on the surface. The sulcus on the inferior surface of the liver in which the gall bladder and cystic duct were normally lodged, contained only a thin fibrous cord, 2 mm. in diameter and 3 cm. in length. It was impossible to dissect out the duct further than the hilum of the liver where it ended in a small knob which was connected also with the hepatic duct. The common bile duct could not be made out, but a well developed papilla of Vater was made out. An unsuccessful attempt was made to dissect up the duct from below. A very fine probe could be introduced for a distance of about 5 mm.

Spleen consisted of five distinct lobes; the largest four of these measured 2 x 2 x .4, 2 x 2 x 5, 2 x 1 x .4, and 5 x 6 x 3 cm. The grayish blue, rather firm lobes were loosely bound to one another. On section the pulp was of a brownish red color, and the Malpighian corpuscles just visible.

Pancreas was rather small. Its position was disturbed by the great dilatation of the duodenum, bringing it further anterior. On section the organ was of a grayish yellow color.

To describe more in detail, the malformation of the intestinal canal: the slightly dilated stomach measures 2 x 6 x 1 cm. The pylorus was normally situated, but was bound to the liver by fine fibrous adhesions; the stomach was also adherent to the spleen and to a portion of the dilated jejunum. A small portion only of the omentum remained attached to the greater curvature of the stomach. At a short distance from the pylorus, the duodenum measures 1 cm. in diameter. It was tightly bound for several centimeters to the under surface of the left lobe of the liver from where it arches back to the stomach. Extending directly downward for a distance of 7 cm. the gut rapidly increased in size, measuring at its lowest point 2½ cm. across. To its left surface, the cæcum and ascending colon were firmly adherent, to its right about 5 cm. of obliterated bowel and several loops of normal ileum. The duodeno-jejunal juncture could not be accurately determined because of the numerous adhesions and the fact that the duodenum was so greatly enlarged that instead of lying retroperitoneal it hung free in the peritoneal cavity and had a short mesentery. The jejunum next folded directly back and widened out into the large loop which occupied the greater part of the peritoneal cavity. It measured 24 cm. in length, and from 3½ to 4 cm. in diameter, and fibrous adhesions bound it to the upper portion of the duodenum. On both sides of this loop, portions of the obliterated bowel were adherent in regular undulations and covered completely by a thin layer of connective tissue. From the blind end of this loop, the small bowel continued as a small, dense fibrous band about 1 mm. in diameter which for a distance of 4 cm. was nothing more than a thin band of fibrous tissue. It then enlarged slightly and through the wall a white opaque mass about 7 cm. in length and 3 cm. across could be seen. This mass was soft and compressible and ended abruptly. The intestine continued as a thin cord 1 mm. thick for a distance of 3½ cm. Here the cord widened into a normal loop 1.7 cm. long and 4 cm. in diameter; it then narrowed down into a solid cord 1 mm. in diameter for a distance of 11 cm. to again widen out into a loop of normal ileum 3 cm. in length, and for a third time became a normal lumen filled with finely granular material. The obliterated portions were solid throughout.

Below this last constriction the bowel was practically normal, except for the adhesions which bound it to the structures mentioned above. The appendix measured 5 cm. in length and together with the ascending and transverse colon was located in the left lumbar region. The sigmoid and rectum were normal.

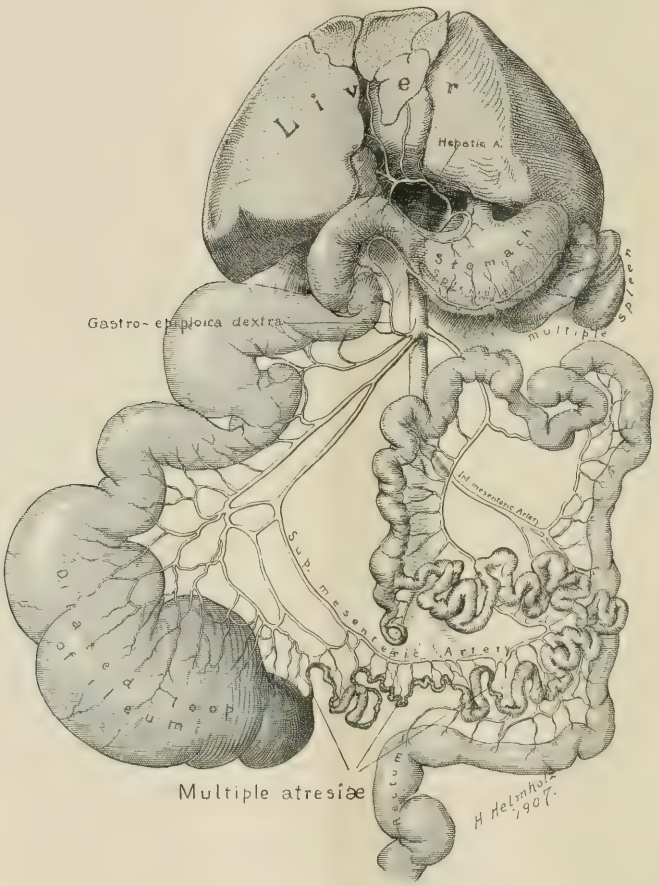
Cultures taken from the intestinal canal below the atresia showed the following:

Rectum at pelvic brim, several colonies, B. lactis aërogenes.
5 cm. above brim of pelvis, negative.
10 cm. above brim of pelvis, negative.
20 cm. above brim of pelvis, negative.
Ileo-cæcal valve, 1 colony B. acid formans.
Just below atresia, negative.
Mid-way between atresia and valve, negative.

The vascular supply.—The aorta was injected just above the diaphragm with vermillion gelatin. Note was taken of only the larger portal vessels, but no careful injection of that portion of the intestinal circulation was made. The cœliac axis came off from the aorta normally and immediately divided into the splenic and hepatic arteries; the gastric branch being given off by the hepatic as the latter passed by the cardiac orifice of the stomach in its course toward the hilum of the liver instead of as normal passing toward the pylorus and then sending back the pyloric branch to anastomose with the gastric. It then divided into a right and left hepatic branch. From the right were given off branches to the deformed gall bladder, to the pylorus and to the duodenum. The splenic artery ran upward and to the left, supplying no branches to the head of the pancreas and only a few small twigs to its tail. Near the spleen, it divided into five larger branches which supplied the larger of the lobes and sent small branches to the several smaller ones. One of the larger branches continued directly to the stomach and formed the gastro-epiploica sinistra which anastomosed with the dextra, a branch of the superior mesenteric. A number of small branches, the vasa brevia, were given off by the branches passing to the several lobes.

The superior mesenteric artery divided into three primary branches between which there were only a few anastomosing branches. The superior branch, a great enlargement of the pancreatic duodenal inferior, supplied the upper portion of the duodenum, and the greater curvature of the stomach, its terminal branch anastomosing with the gastro-epiploica sinistra; so that in this case the gastro-epiploic dextra was a branch of the superior mesenteric, a rather infrequent variation according to Quain. The middle branch can best be considered the continuation of the superior mesenteric, the inferior as the colica media; these two vessels formed one large loop, from which small vessels were given off directly to the intestinal, forming no arches and only

very scant anastomoses. This single vascular loop supplied the jejunum, the ileum, and the ascending and transverse colon. Instead of the 12 primary intestinal branches, the ileo-colic and the colica dextra, the entire number was merged into the single large loop. In the concavity of the largest loop of bowel there was a small plexus which might perhaps be considered an arch; the relations can be best seen by referring to the accompanying figure. The blood supply of the obliterated portion of the bowel differed in no way from that of the remainder of the ileum except that perhaps the vessels are of slightly smaller caliber. At the point where the intestine constricted suddenly to a fibrous cord, the vessels were delicate but quite numerous in the mesentery, and several fine branches supplied the bowel just beyond. Near and at the mesenteric border numerous anastomoses can be made out.



The colica media anastomosed as normal with the colica sinistra of the inferior mesenteric. The remainder of the blood supply to the intestinal canal was normal.

Microscopic Notes.

Lungs contained numerous areas in which the alveoli were filled with an exudate consisting largely of polymorphonuclear leucocytes, and some red blood cells and lymphocytes. The alveolar walls were thickened and congested. Many of the alveoli were filled with erythrocytes and serum.

Spleen.—The venules were distended with red corpuscles, their walls were, however, thin and delicate. The Malpighian corpuscles were normal.

Liver.—Corresponding to the tracery of fine gray lines seen in the gross there were seen bands of young cellular connective tissue running through the liver, for the most part connecting the portal spaces. The distribution of connective tissue was not uniform, but conformed fairly well to the type of annular cirrhosis. In the bands of fibrous tissue there were numerous lymphocytes and polyblastic wandering cells, and some proliferating bile ducts. The liver cells were swollen and fatty. In the hepatic capillaries were numerous blood-forming islands characterized by the small opaque nuclei tinged with hæmoglobin. A few club-shaped enlargements composed of liver cells with large vesicular nuclei were found. In the capillaries an occasional multilobulated nucleated cell of the megalokaryocytic type was seen.

Several sections through the fibrous strand (the remains of the gall bladder) showed that it consisted of a mass of fibrous tissue

in which were to be seen several cysts lined by cuboidal epithelium. No recent inflammatory tissue was made out.

Pancreas.—The arrangement of the lobulation was irregular because of a marked increase in fibrous tissue and the degeneration of the parenchyma. The islands of Langerhans were small and inconspicuous.

Kidneys.—The organs were congested, and at some points showed small hæmorrhagic areas. The epithelium was granular, but otherwise normal. At the cortex the glomeruli were still budding. The usual uric acid infarcts were found in the pyramids.

Thyroid.—The gland shows the same congestion that was everywhere seen and also a decided increase in fibrous tissue.

Testes were normal.

Intestines.—I. Serial sections of tip of large loop and first constriction.[1] The wall of the distended loop, in spite of its enormous enlargement, showed fairly normal structure. The epithelial lining had for the most part disappeared, but the villi had not been obliterated by the tension. At the point in the large loop that was continuous with the obliterated cord there was a small, shallow depression in the submucosa. The mucosa was, however, continuous over it, and did not extend into the fibrous mass. As compared with the normal intestine the muscular coats were slightly hypertrophied; both of the muscle coats of the obliterated portion were continuous with those of the dilated loop. The submucosa of the atrophic part consisted of a solid mass of cellular connective tissue, rich in vessels, but lacking an epithelial lined lumen. The slight enlargement seen in the gross as a white opaque mass proved microscopically to be an encysted cavity filled with a thick granular material that stained a uniform deep bluish purple with hæmatoxylin. No epithelial lining could be made out in the cavity, its wall consisted of a rather cellular connective tissue densely infiltrated with lymphocytes and a lesser number of leucocytes. The series of microscopical sections showed that the lumen did not extend out into the obliterated portion, but occasional small masses of this same material were found embedded in the wall of the cavity and for a short distance beyond at either end.

II. Serial section of a normal loop obliterated at either end. The conditions were essentially the same as in the first constriction. The mucosa was thrown up into typical valvulæ conniventes, shorter and broader than normal. The submucosa and muscular coats appeared normal. The lumen of the loop was filled with pink granular material. At neither end did the lumen extend out into the atrophic cords. At the one end, there was a small cup-shaped depression of the mucosa, at the other the mucosa does not even show this slight irregularity. The obliterated portions showed in none of the sections any sign of epithelium.

III. Cross sections of a small portion of the obliterated bowel. The series was cut especially to determine whether or not small islands of epithelium remained in the cord; in no section, however, were any epithelial cells found. Fibrous tissue had invaded the muscular coats surrounding the small central area of submucosa in which were several alveoli lined by flat endothelium and containing in some instances injection material. These were in all probability vascular spaces.

CASE II.—Baby A. Aet. 3 days. Died February 1, 1906.

Clinical history.—The infant was brought in 43 hours after birth because of the vomiting of bile stained mucous. It was the child of a healthy mother. The child was born at term, the only abnormality was a possible hydramnios. At the birth the abdomen was markedly distended, to relieve which it was given castor oil, and later sugar water. Large amounts of thick, dark green material were vomited shortly after birth; no blood was seen in the vomitus. The distention gradually increased and the bowels remained obstipated.

Physical examination.—The child was small and poorly nourished, its feet and hands were cold, and its pulse very weak. During the examination, the infant vomited 50 cc. of dark green fluid. No external malformations could be found. The abdomen was markedly distended, the veins were enlarged, and the skin cyanotic. No peristaltic waves were seen, nor masses felt. The walls were extremely tense. No dulness could be made out in the flanks. The anus showed no staining from meconium.

Operation.—January, 31, 1906, 10 p. m. The right rectus was incised and an opening made directly into a large cavity containing a considerable amount of greenish gray material, resembling meconium. At the lower end of the abscess cavity was a small opening leading into the general peritoneal cavity. Several enormously distended loops of intestine were traced down and were found to end blindly. A tube was sutured into the blind end of the intestine, and the large cavity packed and closed. The child died several hours after the operation. A complete section was not allowed, so the abdominal cavity was examined through the operation wound.

Anatomical diagnosis.—Congenital atresia of jejunum; diphtheritic enteritis with abscess formation; secondary inflammatory atresia; acute peritonitis.

The peritoneum was deeply injected and covered by fibrous adhesions. There was a slight amount of turbid fluid in the cavity.

The liver was of a purplish color, smooth on the surface and of normal consistency.

The stomach and duodenum were slightly distended, but otherwise showed no abnormalities. The jejunum, greatly distended so that in its widest portion it measured 1 cm. in diameter, ended blindly in a sac, which was of smaller diameter than the bowel some distance above it and was situated 50 cm. below the duodeno-jejunal juncture. The vascular distribution could not be worked out. Tracing the lower portion upward the rectum, sigmoid, and colon were collapsed and the appendix normal. Passing along the ileum upward from the ileo-cæcal valve, it was found to be twisted and its mesentery of very uneven length. The canal was patent up to within about 10 cm. of the large abscess cavity, that had been cut into at the operation, and was found to connect directly with the distal portion of the bowel. The constriction measures only about a millimeter in length, and had very much the appearance that would be produced by tying a string around the gut. It was impossible to pass a probe through this constriction. Above this point the intestinal walls were hypertrophied and thickened, and on passing upward gradually increased in diameter until the canal finally widened out into the lower posterior part of the above described abscess cavity.

This cavity was situated just behind the abdominal fascia and recti muscles, which formed its anterior wall. The remainder of the wall was made up partly of the dilated bowel and of fibrous tissue, the distinction between the two being hard to make out as the wall was for the most part necrotic and the muscular coats had in great part been displaced by fibrous tissue. No communication with the umbilicus, round ligament or urachus was made out. When collapsed, the cavity measured 8 x 7.2 cm. The wall was thin and elastic, and its inner surface was lined by a shaggy greenish, necrotic-looking membrane. To its posterior wall, the omentum was adherent, and also to the tip of the gall bladder.

The bladder and kidneys were normal.

The thorax was not examined.

Microscopical examination.—I. Serial sections of atresia below abscess. The intestinal canal above the atresia was lined by normal mucous membrane, thickened on the mesenteric border, and thinned out and compressed along the free border. The crypts of Lieberkühn along the latter border lay parallel to the wall; on the opposite side they formed a thick mass in which

[1] The series was unfortunately incomplete, so that only the grosser structures could be followed through.

there were numerous small cysts. The muscular wall showed the same relative condition, being two to three times as thick along the mesenteric border as along the free where the two muscle layers were often fused and indistinct. The serosa was greatly thickened by a large layer of cellular fibrous tissue in which numerous groups of lymphocytes and masses of yellow pigment were found.

In the serial sections the lumen gradually narrowed down, the same relation of thinned wall and compressed mucosa persisting. Little by little there developed an enlargement along the mesenteric border in the thickened muscle, forming a large mass in which the muscle fibers were arranged concentrically, and the center of which was in a section further along formed of loose fibrous tissue in which an epithelial-lined lumen gradually made its appearance. The muscle mass showed also the two distinct layers by this time. As the one lumen grew, the other diminished in size. There was no atresia, however, as was at first supposed. The lumen was continuous through the constriction, but was so flanked on both sides by valves made of fibrous tissue projections of the submucosa that any increase in pressure from above would only tend to obstruct more completely the thin slit-like channel.

To explain more in detail the arrangement of the valves. The two lumina lay side by side, and from one side of one and the opposite side of the other project folds of submucosa reaching almost across to the opposite side and having between them a slit-like epithelial lined lumen. This was, however, not complete throughout its entire length and ended in a mass of mucosa. Down to the point at which the upper lumen entirely disappeared the same relation holds true until finally the epithelial-lined lumen became only a mass of epithelium, still protected by a large single valve. As the pressure above increased the tendency would have been to more completely block the slit by the apposition of the valves.

II. Serial sections of the atresia above abscess.[2] The series demonstrated very clearly that the obliteration of the lumen was not a congenital malformation, but was secondary to an inflammatory process. The first sections showed the ileum to be a considerably dilated tube, the walls of which were hypertrophied and thickened by a great increase in fibrous tissue. The muscular coats extend only one-half way round the lumen, and then abruptly shade off into a mass of fibrous tissue which forms the entire thickness of the other half of the wall. The mucosa, submucosa, and muscular coats here have undergone complete necrosis, the remains of the muscular coats could just be made out by their arrangement in the peripheral portion of the necrotic zone, which was separated from the fibrous tissue by a zone that is thickly infiltrated with polymorphonuclear leucocytes, and red blood cells. The lumen at first was an irregular slit about 3 mm. in length, about three-fifths of which was lined by almost normal mucosa, the remainder by a necrotic diphtheritic membrane including practically all that remained of the normal intestinal wall. A portion of the lumen toward the normal side then became constricted, continuing as a round lumen, and gradually disappeared from the sections.

The lumen became still further constricted by the bulging inward of the diphtheritic membrane, converting it into a crescent-shaped slit. Continuing the series a larger and larger portion of the wall became involved in the process and finally the entire mucosa was replaced by a necrotic diphtheritic membrane, which was completely surrounded by a dense mass of fibrous tissue. There remained a small amount of smooth muscle lying somewhat apart, however still showing the circular layer and the longitudinal running at right angles to it and surrounding it on two sides. About ten sections further along the last traces of muscle have disappeared. The lumen by this time was obscured and practically obliterated by a mass of necrotic material infiltrated by leucocytes. In the surrounding connective tissue there were many polyblasts loaded with blood pigment, and also some small hæmorrhages. At one point the necrosis extended almost to the peritoneal surface. Still further along the lumen became entirely obliterated by the ingrowth of connective tissue and only remained as a solid mass of acute inflammatory tissue with a central hyaline mass of necrosis; this later faded out into a delicate fibrous tissue in which all signs of an intestinal canal are lost. The bowel above the lower atresia was enlarged and the muscle hypertrophied. The mucosa was practically normal except for slight thinning toward one side. There was some variation in the thickness of the muscle layers, especially of the external. Passing upward toward the abscess, the bowel becomes still further dilated, the muscular coats thickened, and the submucosa made up of a delicate fibrous tissue. In the mucosa, there are numerous hæmorrhages. On the serous surface, there was an acute organizing peritonitis which had in places completely destroyed the external muscle layer.

Sections taken through the abscess wall including the cross section of the ileum as it leaves the cavity showed a very marked destruction of tissue. The wall on one side was made up of rather sclerotic fibrous tissue lined by a necrotic membrane; the other side was completely necrotic, showing numerous large vessels filled with red blood corpuscles, and there were also numerous red cells in the tissues suggesting the appearance of an hæmorrhagic infarct. This same portion of the wall helped to enclose on its other side an abscess cavity, the remainder of the abscess wall being formed by two loops of intestine closely adherent to one another. The one intestinal loop has undergone complete necrosis, the other on the side opposite to the abscess cavity has a large necrotic zone replacing the mucosa, and this was surrounded by a muscular layer infiltrated with fibrous tissue. The fibrous tissue contains considerable blood pigment.

The kidney, the only other organ saved for microscopical examination, showed nothing abnormal.

To come back to the etiological factors in the two above described cases. Case I is a very typical case of multiple atresia, as described in a great number of instances, except that the peritoneal adhesions and other signs of infection are more marked features than are usually found. The plate does not give any idea of how the intestinal loops were closely bound by fibrous adhesions, especially the completeness with which the obliterated portions of the bowel were literally plastered to the mesentery of the large loops and covered by a thin layer of fibrous tissue. Other evidence of early fœtal inflammation is the peculiar character of the mesenteric blood supply. As is well known, in the fœtus there are a very great number of anastomosing arches which are gradually obliterated during the fœtal life until the normal number of arches remain. In this case, on account of inflammatory changes, there has been an excessive destruction of arches leaving only a single large loop from which the branches pass directly to the intestine. Whether the change in the blood supply is the cause (as suggested by Wyss) or the result in these cases, can in this instance be settled in favor of the latter. At the point of the uppermost atresia, there is a more

[2] The sections include the portion of bowel just above and the beginning of the obliterated bowel.

nearly normal arrangement of vessels, than almost anywhere else along the course of the intestinal canal and though the vessels are smaller than normal, their caliber is better explained by loss of function of the part than by congenital malformation. A second accessory factor is the well developed cirrhosis of the liver, which can be most easily explained as secondary to the blocking of the bile ducts. A cirrhosis of the annular type, not of syphilitic origin, is a very unusual find in a child at birth. The cirrhosis of the pancreas is best explained in like manner. To determine whether the atresia of the bile duct and bladder was inflammatory or developmental was not possible with any degree of certainty, but with the evidence so marked for a fœtal peritonitis, it seems probable that this obstruction was a part of the same process.

Kreuter, in his article on this subject, makes the assertion that in practically every case the atresia was due to a persistance of the fœtal atresia found normally between the 5th and 10th week. This, however, cannot be considered a cause of the atresia as one would be led to believe, but merely the process by which it takes place, and although it is a step forward in explaining how the atresia may occur, it can hardly be called an etiological factor. That a peritonitis might cause a persistance of the embryonic atresia seems possible, but not probable because of the early stage at which embryonic atresia occurs. How to account for the disappearance of the epithelium without inflammation and necrosis seems a difficult task.

Case II illustrated perhaps better than any case yet described the results which may follow atresia. The lower atresia can most readily be explained by supposing that the valves which practically formed a complete obstruction were produced by an outgrowth of fibrous tissue into a mass of epithelium which for a certain time during the second month occludes the lumen. Kreuter has mentioned the change of character in the epithelium when it grew in solid masses and its resemblance to round cells and its return to normal as soon as lumina were formed. That this is true of adult epithelium as well, can be shown in experiments on the rectal mucosa, epithelial downgrowths taking the squamous type and returning to the cylindrical only when lining a lumen. Secondary to an intense infection which led to the formation of an abscess, a possible infarction and an inflammatory atresia followed in which the process can be definitely traced. This inflammatory atresia is not a single instance, but can be classified with several others reported in the literature. Marchwald reported the finding of cocci with Gram's stain in a mass of hyaline necrotic tissue secondary to a diphtheritic enteritis. Thorel reported ulceration and diphtheritic inflammation, and Kirchner found an enteritis and peritonitis.

The fact that the intestinal canal opened right out into the abscess makes it seem that it as well as the atresia was just part of the general process, a diphtheritic inflammation with perhaps a secondary thrombosis which has completely destroyed the intestinal canal and widened it out into this large abscess cavity on the one hand, and on the other led to an atresia.

In summing up the etiological factors in 185 reported cases of congenital atresia of the small intestine, Kuliga disputes in turn the bearing of each one of the described etiological factors, but he has no explanation or explanations to offer in their stead, and leaves one in a very uncertain state of mind when one gets to the end of his article. It seems of greater value to explain the facts as logically as possible, with the known factors, rather than give no explanation at all. Since Kuliga's summary there have been fourteen cases reported, including the two herein described. Case III of Chiari's series is of interest because of the necrotic intussusceptum found on microscopic examination. Howell found that the distal portion of the bowel had intussuscepted itself for a distance of about two inches. Karpa also gives fœtal intussusception as the cause of the obliteration found in his case. Wernstadt explains the atresia in his case by the persistance of the embryonic intestinal atresia. In two of the other cases Edington and Clogg, Case I, give excessive obliteration of Maeckels' diverticulum as cause of the atresia. In the six other cases no definite etiological factor is given.

Thus in 14 cases three (21 per cent) are reported definitely due to intussusception, which is a large percentage when compared with one per cent in Kuliga's statistics.

In conclusion it is urged that more complete histological studies be made in all cases, so that the relative importance of the various factors be determined. I should like to thank Dr. Whipple for turning these two interesting cases over to me, and Dr. Sowers for his notes on Case II.

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A SYNCYTIOMATOUS TUMOR OF THE STOMACH.

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The very interesting histological features of this tumor of the stomach, made it seem of sufficient value to report it as an individual case. Though in all probability a number of similar cases have been reported, it is impossible to cull them out by the titles given in Catalogue of the Surgeon General's Library. This tumor has been called *syncytiomatous* because of its resemblance in many areas to syncytium, in the hope that until a better term is applied, the cases of this kind may be brought together under this head.

Clinical Note.—L. M. Black. Aet. 40 years. Admitted October 29, 1906, to the Johns Hopkins Hospital, complaining of pain in stomach.

Past history.—Constipated for many years. Syphilis at 24. Lost 36 pounds in last year.

Present illness.—During September patient began to feel poorly and lose his appetite. On October 1, 1906, while at supper, had a sudden stabbing pain in the epigastrium and feeling of nausea. After vomiting pain ceased. For five days vomited about one-half hour after each meal. No pain after eating since.

Physical examination.—Marked fullness of epigastrium extending to within 3 cm. of ensiform cartilage; definite edge to be made out. Spleen 2 cm. below costal margin. Test meal: Free HCl. No sarcinæ or yeast cells. On surface to right large nodules are distinctly palpable. In the mid-line the liver extends 14 cm. below the tip of the ensiform.

Clinical diagnosis.—Abdominal tumor (liver?), lues (?), cancer (?).

The post-mortem examination was made two hours after death. The section was No. 2807 of the Johns Hopkins Hospital pathological series.

The anatomical diagnosis was: Syncytiomatous tumor of stomach; metastases to gastro-hepatic, mesenteric, anterior mediastinal glands, liver, spleen, and lung; direct extention to pancreas and colon; ascites and generalized peritonitis; chronic fibrous myocarditis; calcified sub-pleural tubercle; chronic fibrous pleuritis of left side; acute interacinar pancreatitis; chronic diffuse nephritis; chronic lepto-meningitis; ossification of falx cerebri.

Body is that of a very emaciated negro, measuring 167 cm. in length. The body is still warm. Rigor mortis marked. The pupils are equal and dilated. The abdomen is markedly distended, and in the left hypochondriac region a firm, hard mass can be felt. On opening the peritoneal cavity about 1200 cc. of yellow turbid fluid, containing numerous shreds of fibrin were obtained. Everywhere the peritoneal surfaces are covered by small shreds of fibrin. The liver is enormously enlarged, extending 10 cm. below the costal margin in the right mamillary line, in the mid-line 19 cm. below the xiphoid cartilage, and in the left mamillary 8 cm. below the margin of the ribs. The gall bladder is exactly in the mid-line. The surface of the liver is very irregular, showing numerous white and a few reddish elevations, its superior surface is bound down to the parietal peritoneum, and to the diaphragm by a mass of rather firm fibrous adhesions. In the suspensory ligament and in the parietal peritoneum there were several firm, yellowish gray nodules of the same general character as those in the liver. The enlarged liver has displaced the stomach downward into the lumbar region, where it forms a large firm mass, adherent to the colon and the retroperitoneal structures. The spleen is everywhere bound down tightly by adhesions. On the right the diaphragm extends to the fourth rib, on the left to the fourth interspace. The right pleural cavity is completely obliterated by dense fibrous adhesions, the left is entirely free. In the pericardium there is a slight excess of clear straw-colored fluid.

The *heart* is slightly enlarged, weighing 300 gm. Its surfaces are everywhere smooth and glistening. On the posterior surface of the left ventricle there is a large yellowish gray patch, measuring 3 x 1½ cm. On opening the heart the valves are all found delicate and competent. The right ventricular wall measures 5 mm. across, the left 2 cm. Extending from the septum to the papillary muscles in the left heart are several moderator bands, and from its upper portion extends a muscular bundle 5 mm. thick to the anterior wall, arching through the cavity. The posterior wall of the left ventricle has a rather grayish appearance, and is considerably thinner than the rest of the ventricle. On section it measures 4 mm. across and consists to a large extent of only fibrous tissue. The base of the aorta is markedly sclerotic, especially about the orifice of the coronaries. The opening of the right cannot be made out, as it is involved in a thick, yellowish gray patch of sclerosis. On passing a probe through the coronary from a distal point, it emerges in a small slit right in the middle of the patch. The coronary vessels also show marked sclerosis.

Lungs.—The right lung is collapsed and everywhere covered with shaggy adhesions. At one point along the anterior margin there is a fibrous thickening, partially calcified and containing thick granular material. Several other small grayish nodules are seen on the cut section. The bronchi and larger vessels at the hilum are clear. The left lung is smooth on the surface and on section is of a pinkish yellow color, and shows no areas of consolidation.

Spleen measures 9 x 5½ x 2½ cm., and weighs 95 gm. The organ is of a grayish blue color and its capsule is wrinkled and covered by old fibrous adhesions. On section there is a slight increase in fibrous tissue, the Malpighian corpuscles are just visible, and at one point there is a small grayish granular nodule measuring 4 cm. in diameter.

Kidneys weigh 250 gm. The left kidney measures 10 x 7½ x 2½ cm. The capsule strips readily, leaving a uniform yellowish red surface, on which the dilated stellate veins, and small red retracted patches stand out very prominently. On section the cortex measures 6 cm. across, and the striations are quite regular. The right kidney measures 9½ x 5½ x 2 cm. The capsule strips readily except at one pole where it is firmly adherent to a large depressed area. On section of this area the striations and glomeruli are absent, and the cortex measures but 1 cm. across.

Stomach measured roughly 17 x 7 cm. The organ is firmly bound to the retroperitoneal structures and colon. The tumor involves the pyloric antrum and the lesser and greater curvature for a distance of about 10 cm. The mass is exceedingly firm and hard; the anterior wall does not collapse on allowing the air to escape from the stomach. Situated in the lesser curvature are several large, firm, yellowish glands, and one large reddish yellow mass, measuring 5 x 4½ x 3½ cm. and of very much softer consistency than the yellow nodules. Hanging from the greater curvature near the cardiac end there is a similar reddish-yellow mass, which measured 5 x 3½ x 2 cm., and resembled the one in the lesser curvature. On opening the stomach along the greater curvature the tumor is seen to involve the stomach 12 cm. inward from the pylorus and completely encircles it. In the central portion of the tumor is a large ulcerated area measuring about 3 cm. across; its base is clean and smooth and mottled red and yellow,

its edges are smooth and rounded off. Extending outward in the submucosa from this central area are numerous finger-like processes, which gradually shade off into the normal stomach wall. In several spots over these processes the mucosa has been destroyed, leaving small ulcerations which, like the large ulcer, have a smooth base and clean rounded edges.

The thickness of a cross section of the tumor in the central ulcerated area is ½ cm., and toward the periphery shades off gradually into the normal thickness of the stomach wall. The tumor consists of irregular lobulations of varying shades of yellow and gray, alternating with dark red, apparently hæmorrhagic, areas. Definite distinction between epithelium and stroma cannot be made out. The entire mass has the appearance of a uniform tissue in which necrosis and hæmorrhage has produced a variety of colors. The more peripheral portions of the tumor on section are of an opaque grayish color and can be seen invading the submucosa and muscular coats. The large masses at the lesser and greater curvature on section are of a uniform pinkish yellow color, and at their margins show numerous hæmorrhagic areas. Section of the other nodules show them to be of a uniform grayish yellow color, rather granular and friable, and presenting some areas of softening.

Pancreas is firmly adherent to the tumor mass, and also to the large mass at the lesser curvature. The organ has been invaded along its middle third, without any very deep extention down into it. The tumor tissue, of a mottled grayish white and reddish color, stands out sharply from the translucent pinkish yellow pancreatic parenchyma. The organ is otherwise normal.

Liver is greatly enlarged, measuring 24 x 30 x 11 cm. and weighs 4070 gm. Its surface is covered over by a thick coating of fresh fibrinous adhesions, and is studded with metastases which are of two distinct types: the one rather firm, of a uniform yellowish gray color, and irregular edge, the other soft and elastic, of a reddish brown color with occasional yellowish gray area in it. These metastases vary in diameter from 1 to 2½ cm. In the folds of the suspensory ligament and adherent to the gall bladder there are found several yellowish opaque metatastic nodules. On section metastases thickly stud the liver substance, involving more than half of the surface. The metastases have the same character as those described on the surface. The yellow type is much the larger in size, one conglomerate nodule measuring 5½ x 6 cm. The center of the larger nodules has become softened and necrotic, and in some only a few strands can be seen passing across the depressed necrotic center. The nodules are evenly finely granular, and no definite stroma can be made out; there is, however, a slight lobulation to be made out in the larger nodules. The brownish red nodules show a more definite arrangement. There is a rather coarse network of pinkish yellow anastomosing bands of stroma dividing the growth into various sized lobules of a deep reddish brown color. There are all transitions between the two types of metastases. The small 1 cm. nodules also show the two types, so that the one cannot be a degeneration of the other. The liver tissue is of a yellowish brown color, the lobulation well marked by a slightly redder tint of the central portion of the lobules.

On the wall of the portal vein, numerous small metastic nodules are seen, sometimes as a large single nodule measuring 1 to 2 cm. across, or as a little cluster of pin-head-sized nodules covering an area of about 5 x .3 cm.

Intestine.—The small intestine is practically normal; the large intestine, except for adhesions to the tumor in the transverse colon, is the same.

Bladder, prostate, seminal vesicles and *testes* normal.

Aorta shows very marked arterio sclerotic thickenings. In the abdominal aorta the process has gone on to calcification and ulceration.

Brain.—The pia arachnoid is greatly thickened over the cortex, especially along the longitudinal fissure. The falx cerebri is almost completely ossified.

Microscopical Notes.

Heart.—The muscle fibers are hypertrophied, but in areas have undergone a granulative degeneration and have been replaced by fibrous tissue. The endocardium is considerably thickened.

Lungs.—The alveoli are free of exudate and the lungs, except for several tumor metastases, are normal. These nodules are found exclusively in and extending out from the blood-vessels. Quite a number of the smaller arteries are plugged by masses of tumor cells and one vessel is lined by tumor cells, but still contains red blood corpuscles. The largest of the metastases is in connection with a large vessel which is completely filled up with tumor cells. The metastasis shows several areas of degeneration, and the cells contain large and irregular nuclei. At one end is a thin, crescent-shaped space, which is all that remains of the lumen of the vessel. The tumor spreading out into the alveoli has an irregular alveolar arrangement without sharp definition between stroma and tumor cells. In this area are several vessels stuffed with tumor cells. The cells are very irregular in size and take almost any shape. Their nuclei vary greatly in size; a large, spindle-shaped, vesicular nucleus is the most common, but large masses of nuclear material and giant cells are seen.

Spleen.—The capsule and trabeculæ and also the walls of the venules show an increase in fibrous tissue. The change is noted in the Malpighian corpuscles. The metastases are very small, and for the most part seem of very recent origin, in that they lie free in the blood spaces in small groups of from ten to a dozen cells. The individual cells cannot be distinctly recognized, and no stroma can be seen in these small metastases or in the larger one. A single mitotic figure was found.

Pancreas.—The pancreas is compressed and invaded by the tumor growth. Throughout there is an increase in the connective tissue, especially marked toward the tumor. In one portion the pancreatic parenchyma is undergoing a rapid degeneration; there is a great out-wandering of leucocytes and lymphocytes into the acini. The white blood cells are especially numerous along the newly developed strands of fibrous tissue. In one acinus as many as 20 polymorphonuclear cells are crowded; the epithelial cells are either drawn out and atrophic, or have entirely disappeared. In other areas portions of acini have undergone hyaline necrosis. Lying free in one of the larger splenic veins are a group of tumor cells. The islands of Langerhans are unchanged.

Kidney.—The cortex is irregular and consists in the depressed areas of a cellular vascular connective tissue in which some few sclerotic glomeruli and atrophic tubules remain. The convoluted tubules are swollen and contain granular material, their epithelium shows parenchymatous degeneration. The renal arteries show a marked degree of thickening. No tumor metastases are found.

Aorta.—The intima is enormously thickened and degenerated. Over a large portion of it there is a fresh thrombus mass. The greater part has undergone necrosis, showing no nuclei, but great numbers of cholesterin crystal spaces. The middle of the ulcer, in a little cup-shaped depression, has extended through almost the entire wall of the aorta. It is covered over by a calcified plaque, separating this secondary degeneration from the rest. The media further shows numerous areas of cellular infiltration, extending through its entire diameter. The lumina of the vasa vasorum are in many of the vessels almost obliterated.

The *adrenal* appeared normal.

Stomach.—Sections taken through the tumor in the ulcerated area show that practically the entire wall is made up of tumor cells, leaving only a few muscle bundles intact. The mucosa narrows down somewhat and is infiltrated with lymphocytes, but

otherwise is perfectly normal, even up to the very edge of the ulcer. The epithelium shows no signs of a malignant change, and the edge of the ulcer is thin and delicate, showing no changes similar to those seen in the rolled-over edge of a carcinomatous growth. In another section the mucosa overhangs the tumor growth for a short distance, and nowhere shows anything but normal cylindrical epithelium. At a short distance from the ulceration there is an invasion of the mucosa by the tumor, which breaks through the muscularis mucosa. The mucosa in its lower portion consists of a small mass of tumor cells, which have almost entirely destroyed the gland tubules, between which they grow up almost to the surface. The cells are very irregular in their character, a number of acini having the light staining reaction of the hypernephroma cells. The tumor cells have extended almost to the surface and would soon produce an ulceration in much the same manner that the others were no doubt produced. At another point a little further along the growth has extended through the muscularis, but has not invaded the mucosa. In sections taken from the more outlying parts of the tumor the mucosa is everywhere normal.

The tumor apparently originates in the submucosa or muscularis, as nowhere can any relation be made out to the gastric epithelium. In the central portion of the tumor, submucosa and muscular coats are not distinguishable, the entire wall consisting of tumor tissue which shows great variation in its structure. A striking feature is the amount of degeneration that is present, though not surprising on account of the slight amount of stroma that is present in the tumor.

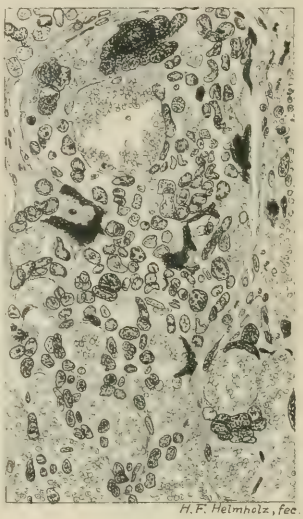
Bands of connective tissue divide the tumor into irregular lobules, which differ considerably in character. The larger part consists of rather irregular sized cells of distinct outline, containing large nuclei, often several, sometimes vesicular, sometimes pyknotic. From this general type there are all transitions to areas in which there are no cell outlines whatever, the protoplasm forming large pink masses, containing nuclear masses which consist of anywhere from 5 to 15 nuclei, that vary greatly in size, some being small and deeply staining, others light with only a few chromatin granules. Only a few mitotic figures are found in such areas, and the frequent areas of necrosis are a further proof that some of these changes are degenerative. Some of these large cells appear to have large nuclei that are not formed by nuclear apposition and they can often be seen lining capillaries.

The relation of the tumor cell to the circulation is very intimate. All through the tumor, usually in lobules, there are blood spaces that are lined directly by tumor cells. This is true not only of the large spaces in the epithelial masses, but also of the capillaries that run in the stroma. They are lined on one side by a normal looking endothelial cell, on the other by a multinucleated mass of protoplasm, and some areas are made up entirely of small vessels lined by tumor cells, and often partly filled with tumor cells.

Quite as characteristic as these are other areas in which the tumor cells take on the type of fibroblasts, forming large, thin-drawn-out cells that run together in bundles, and show all the transitions to the ordinary fibroblast. These areas form only a small part of the growth and are found in the lower portion of the tumor. Mallory's connective tissue stain shows that there are but very few connective tissue fibers in these areas. One area in particular is of interest because of the very great size of the cells, their enormous nuclei in some instances being multiple nuclei. Their protoplasm stains pink, is slightly granular, and shows no striations.

Extending outward in the submucosa, the tumor has markedly involved it and the muscular coat for a considerable distance. The character of the growth is very different. It has grown in small solid acini, as a rule, consisting of from four to ten cells and occasionally in larger epithelial masses. The cells show the same tendency to form multinuclear cells.

Liver.—The liver metastases not only repeat in every detail the original growth in the stomach, but accentuate more distinctly the difference of arrangement described above. In particular are the vascular relations well shown; very peculiar pictures are seen, such as a blood-vessel about 30 mm. across crowded full of red cells, and apparently surrounded by a single cell, the nucleus of which is enormous, extending almost one-half way around the vessel. The accompanying drawing is taken from the same metastasis. It shows the intimate relation of tumor cell and blood current, large multinuclear cells lying practically free in the vessel. The large pyknotic masses of nuclear material are a very prominent feature.



Some areas have a very definite alveolar arrangement, more so than the original growth.

The necroses are also very much more extensive; almost the entire metastasis in some instances is necrotic, only the outer margin remaining intact. As seen in the gross, there is a vein completely occluded by tumor cells.

The liver is markedly congested and the cells atrophic.

The individual cell characteristics are very varied; the predominent cell is a rather small cell with a large nucleus, without any very definite cell outlines, forming irregular masses of cells, the nuclei of which often are massed together to form large clumps. A fine stroma pervades the growth. Mitoses are very frequent; especially large and irregular ones are seen along the margin of several of the small metastases.

The classification of this tumor offers some difficulty. At the post-mortem examination it was supposed to be a carcinoma, with very unusual hæmorrhagic tendencies; the microscopic examination, however, did not support this view.

The edge of the ulcer was slightly overhanging, and the epithelium of the mucosa had no relation whatever to the tumor. Several other invasions of the mucosa show how in all probability the large central, and the many smaller ones were produced.

The microscopic examination showed a tumor that was not to be sharply classified as carcinoma or sarcoma. The cells, al-

though they resembled epithelial cells, were not sharply defined, and had the tendency to form masses and groups which seemed to run together to form large multinuclear cells, and large deep blue staining nuclear masses. In their relation to the circulation they could only be compared to endothelial cells, as they definitely line blood spaces and capillaries, and apparently intermediate stages can be readily found.

The stroma is of very fine character without any definite bearing, except that in several sarcomatous-like areas there appears to be direct transition from tumor cell to fibroblast. The cells show a great tendency to necrosis and the tumor to a hæmorrhagic degeneration.

The metastases resemble carcinoma in that they pass along the lymph channels, and sarcoma in that they have traveled along the blood stream to liver, lungs, and spleen. The vascular metastases in the larger vessels of the liver are of some interest.

The tumor, it seems to the author, may be supposed to have arisen from a misplaced "anlage" in the stomach wall, and because of the syncytial character of the cells may be called a syncytiomatous tumor.

THE RELATION OF INTESTINAL INFECTION TO VISCERAL TUBERCULOSIS.

By G. H. WHIPPLE, M. D.,

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The object of this paper is to present some facts which speak against the theory that the intestinal tract is the portal of entry in a large number of infections with tuberculosis. When such intestinal infections do occur the mesenteric glands are invariably diseased, and when, after a careful examination of these glands, we find them free from any tuberculous process, a definite conclusion may be drawn that the intestinal tract was not the portal of entry.

In a previous communication (1) a series of cases was given in many of which tubercle bacilli were found in the thoracic duct. The intestines and mesenteric glands were examined. The series now numbers 47 cases, and may be grouped as follows:

1. *Acute miliary tuberculosis*—5 cases. Two cases showed vascular foci of distribution, but in addition intestinal ulcers and tuberculous mesenteric glands. The duct smears showed many tubercle bacilli. Three cases showed invasion of the thoracic ducts by the tuberculous process, and the intima in every case was sanded with great numbers of minute tubercles. Duct smears in these cases showed hundreds of bacilli in a single field of the microscope. The first of these three cases presented a caseous salpingitis with extension to the pelvic and retroperitoneal glands, one of the latter rupturing into the receptaculum. The lungs were full of miliary tubercles but there was no cavity present. The second case presented a small plumonary cavity, no intestinal ulcers, but large caseous mesenteric glands, many of them clustered about the receptaculum. No rupture of a gland into the receptaculum was demonstrated. The viscera were full of tubercles. The third case was almost identical with the second, and here the cavity was even smaller, but very rapidly growing with extensive gelatinous broncho-pneumonia. No intestinal ulcers but large caseous mesenteric glands were found.

2. *Subacute tuberculosis.*—(a) 2 cases of Pott's disease of the lumbar region, with involvement of the retroperitoneal glands, and a few disseminated tubercles in the viscera. No lung cavities nor intestinal ulcers. The duct smears were negative although it seems probable that the tubercles in the viscera were due to bacilli which were swept through the duct. (b) 28 cases of pulmonary tuberculosis with cavity formation, and many or few disseminated tubercles in the viscera. Duct smears were positive in 20 cases, at times only two or three bacilli being found after long search, again forty or fifty on a single slide. In these 20 cases the mesenteric glands invariably showed a tuberculous process, usually caseation, while the intestinal tract showed ulcerations in 16 cases. 6 of the 8 cases, which showed no tubercle bacilli in the duct smears, had intestinal involvement, and in all 8 there were tuberculous mesenteric glands. 2 of the cases with bacilli in the duct showed only microscopic disseminated tubercles which were not visible to the eye. This group emphasizes the importance of the thoracic duct as a distributing agent in the cases which show scattered tubercles in the viscera, and tuberculous mesenteric glands.

3. *Chronic tuberculosis*—12 cases of chronic pulmonary tuberculosis with cavity formation, but no disseminated tubercles in the viscera. 8 cases had tuberculous mesenteric glands, while but 5 showed intestinal ulceration. One case showed only two small ulcers in the appendix with a caseous gland at the ileocæcal fold in the mesentery. 4 cases showed neither ulcers nor tuberculous glands.

When one considers the fact that three of this last group were insane patients who swallowed most of their sputum, which was profuse, coming from large apical cavities, that one of the insane cases showed only a small intestinal ulcer, and a caseous mesenteric gland, while another showed only a few tuberculous mesenteric glands and the third no such lesions, it seems clear that the intestinal tract of adults does not absorb the tubercle bacillus very readily. It seems probable that bacilli can pass through a mucosa, which to the eye at least seems intact, but are filtered out of the lymph stream by the glands in the mesentery. These bacilli produce lesions in the glands which plainly mark the course of the infection, and probably the bacilli in the duct smears are derived from these secondary mesenteric foci rather than from the intestine.

During the last 500 autopsies 3 cases were found which showed a calcified mesenteric gland, no intestinal ulcers, a few pigmented fibrous or calcified pulmonary lesions, and tuberculous bronchial glands. In such cases the infection may have been through the intestinal tract, but not surely. When

one considers how common are the findings of healed pulmonary lesions in the routine autopsies, and how infrequent are tuberculous mesenteric foci in such cases, it seems reasonable to conclude that such infections do not take place through the alimentary tract, or at least very rarely. When we study the cases with extensive pulmonary cavities we often find tuberculous mesenteric glands which may be secondary to the pulmonary lesions, or may be primary, and mark the course of an alimentary infection. But comparing this group of cases with that showing slight or early lesions with no pulmonary cavities, we are forced to conclude that the chances are against a primary intestinal infection.

It is of interest to compare this group of cases with a series of hogs in which the distribution of tuberculous lesions was studied. These animals were observed at an abattoir near the laboratory. They averaged from 8 to 10 months of age, 120 to 150 pounds in weight, and were shipped from the middle west where many of them had fed behind cattle. The animals were very healthy as a rule, and the percentage of animals infected with tuberculosis rarely exceeded 3 per cent.

The lesions were usually limited to a few glands, and the cases may be grouped as follows:

1. *Acute miliary tuberculosis*—3 cases. All showed caseous mesenteric and submaxillary glands, the latter often measuring 3 cm. in diameter, and showing complete caseation with slight calcification. The viscera were sprinkled with small tubercles, and the lungs showed small areas of tuberculous bronchopneumonia. One case showed a few small cavities in the lungs, and an ulcer near the cæcum. The ducts could not be examined. Through the kindness of Dr. Mohler, Chief of Pathological Division, Bureau of Animal Industry, I was able to examine five other cases in Washington which resembled closely the cases described. The intestines were not examined, but the submaxillary and mesenteric glands were invariably diseased, and showed the most extensive lesions. The organs showed numbers of small tubercles, and the lungs small patches of tuberculous broncho-pneumonia.

2. *Subacute tuberculosis*—5 cases. All but one had caseous submaxillary glands, and that one showed tuberculosis of the mesenteric glands round the duodenum. Three cases had caseous mesenteric glands. The intestines were not carefully examined, but no conspicuous ulcers were present. The lungs, spleen, or liver showed a few tubercles of varying sizes. No lung cavities were seen.

3. *Local tuberculosis*—14 cases. All but one of these showed tuberculosis of the submaxillary glands, and five mesenteric tuberculosis localized in one or two glands. Such cases make up the greater part of the infections, and many more were seen at the abattoir, but not carefully examined. These animals were all young, and gave an excellent opportunity for the study of the early lesions. Many of them had been fed behind cattle, and probably were infected from them through the food, there being no cases in which the oldest lesion was found in the lungs.

In all cases the channel of infection was marked by a tuberculous gland, either submaxillary or mesenteric. It is remarkable how frequently the submaxillary gland was involved (20 out of 22 cases), and indicates the pharynx as a common and easy portal of entrance for tuberculosis in the case of the growing hog. The findings in this series of cases agree closely with those of Schroeder and Mohler (2), who produced experimental tuberculosis in hogs by feeding. Their tabulated experiments are valuable, and support the conclusions drawn from this work, but their own conclusions are somewhat different. These observations parallel those in children who, it is well known, are more frequently affected with mesenteric tuberculosis (Henke) (3). Children with cervical tuberculous glands in many cases show a tuberculous process in the pharyngeal adenoid tissue (White) (4).

An attempt was made to trace in the common laboratory animals the course of infection from the intestinal tract, and the rapidity of its advance through the mesenteric lymphatics. Owing to an epidemic of pneumonia among the animals used in these experiments the series is incomplete, but the findings will be given briefly as they support the deductions drawn from the preceding cases in men and hogs.

Two cultures of the tubercle bacillus were used in these experiments: one obtained through the kindness of Dr. Theobald Smith—a bovine organism of medium virulence and fairly rapid growth (Bov.). The second culture was isolated from a hog infected with bovine tuberculosis, was of high virulence and slow growth (S.) and was obtained through the kindness of Dr. John R. Mohler. The 27 to 29th generations were used. In order to avoid pharyngeal infection a series of animals (12 guinea-pigs, 7 rabbits, and 3 dogs) were operated upon. The tuberculous material was injected carefully with an hypodermic needle into the stomach or intestines which were sewed to the abdominal wound. In some cases a small opening was made, a capsule of the culture inserted, and the wound in stomach or intestine and abdomen closed tight. In every case it was found that the edges of the wound, however small, in the mucosa, were infected with the tubercle bacillus and the glands draining such areas became tuberculous. In the dogs the mucosa was intact but the mesenteric glands draining the portion of intestine which was operated upon, showed a localized tuberculous process. No other glands were involved. The animals were killed 30 to 35 days after operation. The guinea-pigs and rabbits showed ulcers in the mucosa, a rapid extension of the process through the mesenteric glands, local or general tuberculous peritonitis and pulmonary involvement. The culture (Bov.) was used in all these experiments.

A series of 6 dogs was starved for 4 days—then two capsules (Bov.) and one capsule (S.) were wrapped in a little gauze and pushed far down the œsophagus. They were readily swallowed with no chewing. Each capsule contained the entire growth from a single glycerine agar tube. The animals were then each given one pint of milk. They were killed at varying intervals and the duct contents examined by smears and inoculations. Because of the premature death of the inoculated animals the results are of value only in the cases of 3 dogs.

Dog. 11. Fed as described and killed in 19 hours.

The duct contents: 4 cc. injected subcutaneously in a rabbit; 2 cc. injected intraperitoneally in a rabbit; a suspension made by chopping and grinding up the mesenteric glands in salt solution injected subcutaneously in a rabbit. None of these animals developed any tuberculosis and the glands draining the injected areas appeared normal under the microscope. Smears from the dog's gastric and duodenal mucosa showed a few

tubercle bacilli, from the mucosa of ileum and cæcum many tubercle bacilli. Smears from the duct and mesenteric glands after long search were negative.

Dog 8. Fed as described and killed in 24 hours.

The duct contents: 4 cc. injected subcutaneously in a rabbit; an emulsion of the ileocæcal gland injected subcutaneously in a rabbit; an emulsion of the jejunal and mesenteric glands injected subcutaneously in a rabbit. These animals showed no tuberculous process and their glands were quite normal under the microscope. Smears from the lumina of the dog's stomach, duodenum, ileum, and cæcum all showed a good many tubercle bacilli but smears from the duct and mesenteric glands were negative.

Dog 9. Fed as described and killed in 24 hours.

The duct contents: 7 cc. injected subcutaneously in a guinea-pig; 2 cc. injected intraperitoneally in a guinea-pig. An emulsion of the mesenteric glands injected subcutaneously in a guinea-pig. These animals did not develop any tuberculous process and the microscope showed normal glands. Smears from the dog's ileum showed many tubercle bacilli but smears from the mesenteric glands and duct contents were quite negative.

Dogs 6 and 7. Fed as described and killed in 4 hours. The inoculated animals died the following week (pneumonia). Smears from stomach and duodenum showed many tubercle bacilli, but smears from glands and duct were negative after very careful search.

Three dogs were fed as described and kept as controls but died of a peculiar bronchopneumonia in 2 to 3 weeks. Autopsy showed no lesions of tuberculosis in spite of careful microscopical study of the mesenteric glands.

A series of 4 guinea-pigs (adult) was starved for three days, then to each one was fed one capsule (Bov.); the next day they were similarly fed. Each capsule contained the growth from one glycerine agar culture of the tubercle bacillus (Bov.) and was pushed far back into the pharynx. The pigs could not swallow it without chewing and soiling the mouth and pharynx.

Guinea-pig 34. Fed as described and killed 24 hours after second feeding. Emulsion of duodenal and ileocæcal glands injected subcutaneously into a guinea-pig; emulsion of large mesenteric gland injected subcutaneously into a guinea-pig. The gland fragments wrapped in gauze and planted subcutaneously in a rabbit.

The inoculated animals were killed after 60 days and showed no tuberculosis. Smears from the mucosa of stomach, ileum, and cæcum all showed many tubercle bacilli, but smears from the glands were negative.

Guinea-pig 37. Fed as described and killed 48 hours after second feeding. Emulsion of ileocæcal and duodenal glands injected subcutaneously in a guinea-pig. The large mesenteric gland planted subcutaneously in a guinea-pig. The gland fragments wrapped in gauze and planted subcutaneously in a rabbit. The inoculated animals killed in 61 days showed no tuberculosis. Smears from the ileum and cæcum showed many tubercle bacilli, but smears from the stomach and mesenteric glands were negative.

Guinea-pig 40. Fed as described and fed cabbage leaves 4 hours before killing, 72 hours after the feeding of second capsule. Emulsion and glands treated exactly as in Guinea-pig 37. The inoculated animals killed in 60 days showed no tuberculosis. Smears from ileum and cæcum showed tubercle bacilli, but smears from the stomach and mesenteric glands were negative.

Guinea-pig 43. Fed as described and fed cabbage leaves on 4th and 5th day. Killed 5 days after feeding of second capsule.

The ileocæcal gland planted subcutaneously in a guinea-pig. Half a large mesenteric gland planted subcutaneously in a guinea-pig. Duodenal and half a large mesenteric gland planted subcutaneously in a rabbit. The inoculated animals killed in 58 days showed no tuberculosis. Smears from the cæcum showed tubercle bacilli, but smears from the mesenteric glands, stomach, and ileum were negative.

These four guinea-pigs who had ingested many tubercle bacilli, and were killed 1 to 5 days after such feeding showed no tubercle bacilli in the mesenteric glands, although the bacilli were present in large numbers in the intestinal lumen as shown in smears. Control guinea-pigs which were fed in a similar manner, and killed in 4 to 5 weeks showed caseation of the ileocæcal or duodenal, and mesenteric glands with only occasional small tubercles in lungs, spleen, or liver.

In reviewing these results it must be remembered that a culture of moderate, but not low, virulence was used, and that the dose was not extremely large. It would seem that under such conditions the tubercle bacilli were not swept along through the lymphatic apparatus of the intestine in a few hours, else the control animals would have shown tubercles of equal age in the lungs, spleen, etc., and mesenteric glands. The inoculation animals as well should have shown some tuberculosis, but as the mesenteric glands were free from the tubercle bacilli even as late as the fifth day after feeding, we may conclude that the process is a slowly advancing one. It is possible that by feeding animals with enormous numbers of exceedingly virulent tubercle bacilli, a few of the bacilli may be carried along the lacteals, and pass through the mesenteric glands, into the duct and blood stream, Ravenal (5), Vallée (9), Calmette (10). It seems impossible that the majority of such bacteria could escape the filter of the mesenteric glands where they would lodge, and eventually cause a tuberculous lesion as old as the other lesions—a clear index that the tubercle bacilli had passed along that channel. It seems that such experiments do not closely parallel the conditions in cases of infections in man where the doses are small, and the organism perhaps exposed to factors which tend to lower its virulence. The findings in these cases agree with the recent work on experimental pulmonary anthracosis which was claimed to be alimentary in origin (Calmette and his pupils) (6), but this has been conclusively disproved by Cohn (7) and others. No review of the literature will be attempted, but mention may be made of a paper by Kovács (8) who reviews the recent literature, and outlines the position of the two schools upholding the aspiration, or ingestion theories.

Conclusions.

The tubercle bacillus can not pass from the intestine through the lacteals, mesenteric glands, and thoracic duct into the lungs without leaving some record of such passage. A few bacilli may, under favorable conditions, be swept along this course to the lungs, but the majority surely will lodge in the glands, and in time cause a tuberculous process which can be recognized. When the mesenteric glands are not involved we may exclude the intestinal tract as the portal of entry, but the converse does not hold for the tuberculous mesenteric glands which may be secondary to some pulmonary focus that is discharging tubercle bacilli into the alimentary tract. The thoracic duct is often the distributing agent in cases

which show scattered tubercles in the viscera, and tuberculous mesenteric glands.

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A HITHERTO UNDESCRIBED DISEASE CHARACTERIZED ANATOMICALLY BY DEPOSITS OF FAT AND FATTY ACIDS IN THE INTESTINAL AND MESENTERIC LYMPHATIC TISSUES.

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The following case was characterized clinically by a gradual loss of weight and strength, stools consisting chiefly of neutral fat and fatty acids, indefinite abdominal signs, and a peculiar multiple arthritis. The diagnosis lay between neoplasm and tuberculosis of the mesenteric structures. Pathologically the lesions of interest were found in the intestines and the lymphatic tissue draining this region. The intestinal mucosa showed enlarged villi due to deposits of large masses of neutral fats and fatty acids in the lymph spaces and an infiltration of the interglandular tissue by large mononuclear and polynuclear giant cells. The submucosa in many places shows similar deposit in the enlarged lymph spaces and invasion by large mononuclear cells. The mesenteric glands in gross showed the most striking changes, but under the microscope the picture closely resembled that seen in the intestine. The glands showed the same deposits in even greater amounts, and a chronic inflammatory reaction with replacement of much of the gland tissue by fibrous scar tissue, masses of large mononuclear cells or polynuclear giant cells of the foreign-body type. The lymphatic tissue of the bronchial glands, bonemarrow, and lungs showed no abnormalities of importance. The other organs are described below, but no changes were found which seemed related to the intestinal lesions.

Clinical History.

(58,803), X, physician, æt. 36, single, was admitted to the Johns Hopkins Hospital on April 12, 1907, complaining of "loss of weight and strength; rheumatism; bronchitis; shortness of breath; dilated (*sic*) abdomen; tumor of abdomen."

Family history.—Unimportant. No history of tuberculosis in any branch of family.

Previous history.—Up to five years before the entry the patient had been a remarkably healthy man. Measles and whooping-cough as a child. Chills and fever at 10. Slight attack of pleurisy at 14—in bed only a day or so. In 1899, mild attack of influenza.

Has had some trouble with his nose for which a small portion of each inferior turbinate bone has been removed without benefit. Tonsils were excised when he was a child.

As long as he can remember he has had a slight hacking cough and a desire to "clear his throat." For four and a half years the patient has, he says, had a "bronchitis" with chronic cough, which has always been worse in cold and damp weather.

The patient has been working as a medical missionary in the East, mainly in Constantinople, whither he went in 1899. In his work he has frequently been thrown with tuberculous patients.

The present illness began insidiously, five and a half years ago, immediately on his arrival in Turkey. The first symptoms were attacks of arthritis coming on in various joints. They were transient, the first lasting but six or eight hours. These recurred again and again three or four times a week in damp weather, once a week perhaps, in dry weather, lasting from six to twenty-four hours; rarely severe enough to keep him from work. Nearly every joint has been affected. Sometimes the joints were hot, swollen, and tender; at other times, only painful. Again the pain might seem to be in the muscles; or with pains in the joints there were also pains along the course of both sciatic nerves. The attacks were never associated with fever and on but one occasion were they of sufficient severity to confine him to bed and for but two days. These attacks were associated with a gradual loss of weight and strength. In the course of a year he developed a cough which has continued ever since, varying, however, greatly in severity according to weather and climate—better in dry seasons and climates, worse in damp. This was associated with an expectoration of moderate quantity, of a yellowish color, tenacious and raised with difficulty—more abundant in the morning.

Although gradually losing weight and strength he kept at work, with occasional vacations, until September, 1906, when he came back to America, spending a month in the Adirondacks, where he gained five or six pounds. Thence he proceeded to Atlanta where, in the course of five or six weeks, his cough became much worse, the expectoration increased, and a slight evening fever developed, the temperature rising to about 100°. There were occasional "night sweats" and notable loss of strength and weight. Physical examination showed nothing definite.

Examination of the sputa for tubercle bacilli was negative.

In December, 1906, the patient, fearing tuberculosis, went to New Mexico, where his bronchitis improved. The loss of weight, however, continued, and a diarrhœa set in which has persisted ever since, the stools, from three to four a day on an average, of fluid or semi-solid character. Examination by the patient himself, revealed a deficiency in bile and an excess of fat.

Shortly after reaching New Mexico, three and a half months ago, the patient observed a swelling of the abdomen, which gradu-

ally increased until the circumference amounted to thirty-three inches, since when it has remained stationary. Soon after this a mass became palpable below and to the right of the umbilicus, while there was a still larger indefinite area of dulness and resistance in the same region. There has been some tenderness on pressure in this region.

About *four weeks ago* both ankles, especially the left, became hot, swollen, red, and tender and attempts to walk were painful. This condition, although somewhat improved, still persists.

For the last four or five weeks he has noticed dyspnœa on exertion. The appetite has always been good. No history of jaundice.

Blood Examinations.

April 14. Fresh blood—red cells are pale and irregular in size, there being many microcytes. No nucleated red blood cells. No myelocytes. No marked poikilocytosis.

R. B. C., 4,468,000; W. B. C., 8180; hæmoglobin, 52%.

Differential count:

Polymorphonuclears	410	80.4%
Small mononuclear lymphocytes	16	3.1%
Large mononuclear lymphocytes	32	6.2%
Eosinophiles	47	9.2%
Large mononuclear cells	2	0.4%
Mastzellen	3	0.6%
	510	

April 21. R. B. C., 4,464,000; W. B. C., 8420; Hæmoglobin, 54%.

April 29. R. B. C., 3,932,000; W. B. C., 6780; Hæmoglobin, 53%.

April 30. Coagulation time, 5 minutes 30 seconds.

May 1. Differential count:

Polymorphonuclears	491	89.3%
Small mononuclear lymphocytes	19	3.5%
Large mononuclear lymphocytes	19	3.5%
Eosinophiles	17	3.1%
Mastzellen	1	0.2%
	547	

Examination of Stools.

April 14. Stool is almost white or creamy and has a smooth silky appearance. Under the microscope one sees enormous numbers of fatty acid crystals. They appear as small needle-like crystals arranged in tufts or rosettes which do not stain with Soudan III. This stain shows an abundance of neutral fat in fine globules. Vegetable cells are present and a few pieces of striped muscle. No parasites nor eggs are seen after long search.

Several examinations for tubercle bacilli negative.

April 24. Stool is clay-colored. Microscopically it resembles the ones previously examined with perhaps some increase in neutral fat.

April 28. Stool darker colored. No bile was demonstrable. Fatty acids and neutral fat present in large amounts.

Dr. Boggs. April 20. Stool almost completely composed of split fats and soaps in crystalline form indicating interference with fat absorption. Neutral fat small in amount. Some undigested starch present. Reaction of stool is acid.

Dr. Voegtlin. April 30.

Dried stool, 20 gms. { Neutral fat, 10 gms. / Fatty acids, 6 gms. / Organic salts, etc., 4 gms.

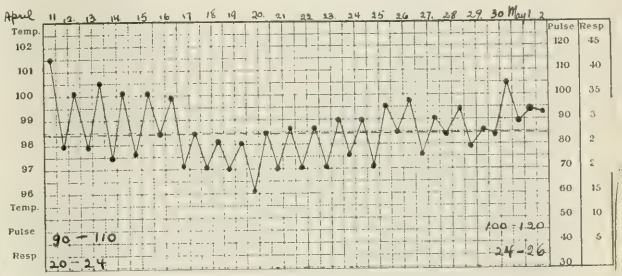
Diet.—While in the medical ward the patient was on a full diet with four raw eggs daily and eight ounces of milk every two hours. In spite of this forced feeding the patient lost weight every week, weighing 145 pounds two weeks before his death. Normal weight, 175 pounds.

Urine Examinations.

April 12. Clear, yellow color. Specific gravity, 1029; acid reaction; no sugar; no albumin; red finely-granular sediment; no casts; many uric acid crystals; diazo negative. Later examinations showed the same general picture.

April 29. Calcium oxalate crystals were present. No bile. *Urine* obtained shortly before death showed the presence of a considerable amount of *acetone* but no diacetic acid.

May 3. .001 gr. of tuberculin was given. No reaction followed. No sputum was obtained except a small amount of clear mucus showing no tubercle bacilli.



Clinical Notes.

Dr. Thayer. April 15, 1907. The patient was thin, and though sunburned was evidently pale. There remained still a good deal of tonsillar tissue with well-marked crypts.

The *thorax* was unsymmetrical, the cartilages of the fifth and sixth ribs of the left side being evidently prominent. The movements of the right upper front were rather freer than those of the left side, and on percussion there was a slight dulness with a trace of tympany in this area. On quiet respiration the inspiration was here a little wavy but no adventitious sounds were heard. Elsewhere, the respiration was clear.

Heart.—Sounds best audible in the fourth space, inside of the mammillary line, about 7.7 cm. from mid-sternal line, at which point dulness begins. Sounds, clear throughout; second pulmonic a little louder than second aortic.

The *abdomen* was rather full. Just to the left of the median line in the epigastrium there was a slight prominence which suggested a small properitoneal hernia. The abdomen was more resistant on the right than on the left, and especially in the right lower quadrant where the fulness seemed more marked; there was a "rather elastic resistance," especially below and to the right of the navel. Tympany on percussion; somewhat duller in the middle of the abdomen and in the left flank. No movable dulness.

The *liver* was not palpable, extending by percussion to a point a little above the costal margin in the mammillary line, and in the median line to a point midway between the umbilicus and xyphoid cartilage. The splenic dulness reached the costal margin but the border could not be distinctly felt.

A few small *glands* were palpable in the axillæ and the epitrochlears were both palpable.

The left *ankle* was swollen, the skin tense and shiny. On the outer side of the foot and on the dorsum there was a diffuse discoloration suggesting old cutaneous hæmorrhage. A greenish-yellow coloration extended from the toes to above the malleoli, while at points there were deeper bluish areas gradually fading into the yellow-green. The ankle was quite hot. On the legs and thighs were a few faded, brown purpuric spots no larger than a pin-head.

In the middle of the left leg, just to the left of the tibial crest,

there was a discolored, greenish, slightly indurated spot having the appearance of a fading patch of erythema nodosum. On the right leg and calf were several similar areas.

Dr. Baetjer. April 17. Radiograph of ankles does not show any bone changes. There is, however, a slight thickening of the periarticular tissues around joints. This does not seem to be tuberculous. No exostosis nor erosion of any bones.

Dr. Barker. April 19. There is a little general pigmentation. Glands in right posterior portion of neck are palpable. Chest shows expansion a trifle better on the right side. There are pigmented moles on chest. Vocal fremitus is normal. Percussion clear. A slight fraction heard in left lower back and a few fine crackles in right supraspinous region. Heart sounds clear. Abdomen full, slightly more marked on right side. Slight tenderness to right of navel. Dulness in right flank; none in left. Slight swelling of left, but more of right ankle.

Dr. Thayer. April 20. Abdomen is a little generally distended and everywhere tympanitic. Less tenderness to-day than last time. There is a muscular resistance to deep palpation in the right upper quadrant just above and to right of umbilicus. No definite mass is felt.

Dr. Baer. April 18. Both ankles are markedly swollen and pit on pressure. There is a slight amount of local temperature, no decided pain on pressure over bones. Dorsal flexion is somewhat limited. Abdomen is much distended with a decided movable mass just below umbilicus.

Dr. Thayer. April 25. Left ankle is not so swollen and looks better. Abdomen is not so swollen—a doughy resistance. Just below navel is felt a nodule the size of a walnut. Palpation here causes a little pain in left side of abdomen. Some suggestion of a lesion at left apex but nothing definite. On deep inspiration in left lower axilla in sixth and seventh interspaces there is an exceedingly soft friction rub—definite in forced inspiration and expiration. This is present also over left lower back, rather more audible than in front. An occasional fine crackle at extreme base of right lung.

Dr. Thayer. April 29. Auscultation of left apex shows a wavy interrupted inspiration but no adventitious sounds. Percussion note a little higher pitched than on right. In the left lower axilla and back a soft friction is audible, reaching to within three finger's breadths of angle of scapula. Over a small area below angle of scapula in right lower back a very rough scratchy friction is heard. Percussion note at both bases is impaired. Heart, no enlargement; sounds clear; pulmonic second sound is accentuated. Abdomen is very full with limitation of respiratory movements, walls not so resistant as before. A rather indefinite tumor felt to right of umbilicus, it is slightly tender. At times to right and above navel a tumor is felt, very movable and rather sausage-shaped.

May 5. Patient transferred to surgical wards for exploration. Operation May 6. No fluid in abdominal cavity. Mesenteric glands very much enlarged and hard. Abdomen was closed. Diagnosis, tuberculosis of mesenteric glands. Patient did well for 48 hours after the operation. He perspired quite freely at times and was troubled with joint pains but slept a good deal. He was on a liquid diet and had frequent enemata, which were not very effectual. Dyspnœa was noticed two hours before death and respirations then numbered 40 per minute; pulse 120.

Dr. Cole. May 8, 1907. The patient was seen by me at 9.30 p. m., at which time he was perfectly conscious, propped up in bed and suffering from extreme polypnœa. The distress seemed to be both with inspiration and expiration. There was only moderate cyanosis, though the skin was cold and clammy. There was no striking odor to the breath. A few râles were heard over both lower lobes, but no areas of consolidation were made out and the condition in the lungs did not seem to be sufficient to account for the extreme grade of dyspnœa. Pulse was rapid, but regular, and of fair quality. He did not seem to be in immediate danger. An attempt was made to have him void as a condition of acidosis was at once suspected and it seemed advisable to obtain some urine for examination. He was unable to void and preparations were being made to catheterize him when he suddenly died.

Clinical Discussion.—*Dr. W. S. Thayer.*

The clinical pictures of this case were in many ways remarkable. The cough, the fever, the progressive emaciation, the abdominal swelling and tenderness, the remarkable character of the stools, indicative of defective fat absorption, were decidedly suggestive of a pulmonary and mesenteric tuberculosis.

On the other hand, the physical signs did not justify a diagnosis of pulmonary tuberculosis and the sputa were negative. The signs at the left apex were interpreted clinically as evidence of an old retraction and not of an active process. Again the blood picture was distinctly not that of a tuberculosis. The anæmia was more marked than common and the eosinophilia present on entry was peculiar. In addition to this were the condition of the ankles with the remarkable history, together with the purpuric manifestations and the areas suggestive of erythema nodosum—symptoms which raised the question as to whether the case might belong to that ill-defined group which has been roughly brought together through the common manifestations of erythema multiforme exudativum and arthritis.

Further examination of the stools confirmed the existence of permanent interference with fat absorption without deficiency in fat splitting or azotorrhœa, while the absence of reaction to .001 tuberculin was strong evidence against the presence of an active tuberculous process.

These observations, together with the result of the exploratory laparotomy led to a final diagnosis of sarcoma or Hodgkins' disease of the mesenteric glands.

It is a matter of great regret to me that I was unable to see the patient after the operation. The remarkable manner of death was as Dr. Cole observed, suggestive of an acid intoxication.

As one looks back upon the history of this case in connection with the remarkable observations at autopsy, it is difficult to resist the conclusion that we are here dealing with a definite and hitherto unrecognized clinical picture with which we shall meet again.

Autopsy Protocol.

Dr. X. Aet. 36 years. Ward C, 2. Autopsy No. 2883. Died 10.40 p. m. May 8, 1907. Autopsy 2 p. m. May 9, 1907. Dr. Whipple.

Anatomical Diagnosis.—Neutral fat and fatty acid deposits in intestinal mucosa, mesenteric and retroperitoneal glands and thoracic duct; chronic lymphadenitis; anæmia; emaciation; organizing peritonitis, pleuritis, pericarditis, and aortic endocarditis; cardiac dilatation and hypertrophy with fatty degeneration; chronic passive congestion of viscera; splenic tumor; hyperplasia of bonemarrow; cloudy swelling

of viscera; laparotomy wound; bronchopneumonia and œdema of lungs; caseous apical scar and tuberculous bronchial lymphadenitis.

Body is that of a well-developed, large-framed, white male, 180 cm. in length. Rigor mortis well marked. The skin of the face and hands shows a deep brownish pigmentation (sunburn). The skin over the trunk and limbs shows no excess of pigment. Over the dorsum and lateral aspect of the left ankle and instep are several diffuse purple spots and the joints show a boggy swelling. The abdomen is slightly distended, shows a recent surgical incision about 10 cm. in length closed by silver sutures just to the right of the umbilicus. The abdomen on incision shows a slight excess of slightly turbid yellow fluid. The intestinal coils are moderately distended with fluid and gas. The loops of ileum and the cæcum are adherent by rather elastic, but easily torn adhesions to the under surface of the scar described above. The peritoneal lining everywhere has lost its gloss and is covered by grains and shreds of moist thready tissue. This exudate is quite well marked in the pelvis where the threads are quite conspicuous and cannot be separated from the intestinal coat without considerable force. The same milky adhesions are present over the spleen and liver. The appendix is clear.

Thorax shows both pleural cavities to be invaded by this same type of inflammation. The cavities contain a little excess of fluid and the serous surfaces are frosted over by these rather elastic moss-like gray adhesions which are most conspicuous over the diaphragmatic surfaces and the posterior portion of the lower lobes. The fat in the region of the mediastinum shows numerous ecchymoses. The pericardial cavity is everywhere obliterated by elastic gelatinous-looking adhesions, in which new-formed blood-vessels can be seen with great distinctness. No fresh fibrin is found anywhere. The two layers can be separated with some difficulty, showing ecchymoses here and there.

Heart, together with the pericardium, weighs 680 gms. It is dilated and hypertrophied. The right auricle shows some dilatation with firm pale gray clots. The tip of the auricle is clear. The tricuspid valve measures 15 cm. in circumference. The valve leaflets are delicate. The pulmonary valve is normal. The intima of the right heart is thin and smooth, through which one sees well-marked mottling of the muscle columns with yellow flecks. The left auricle is moderately dilated, its intima smooth. The mitral valve measures 12 cm. in circumference, and is delicate. The aortic ring measures 8 cm. in circumference. Two of the cusps are normal. The third cusp situated posteriorly and just above the anterior curtain of the mitral valve shows a small sessile vegetation 6 mm. in long diameter, situated on the line of closure close to the Corpus Arantii. It is of an opaque yellow color on its upper portions, but its base shows invasions by delicate capillaries growing up from the base of the valve. The intima of the left heart is smooth and the muscle shows through it, of a brownish color, mottled with yellowish flecks. The coronary vessels show a few patches of sclerosis. The heart muscle is pale and flabby and of a mottled yellowish-brown color on tangential section. The wall of the left ventricle averages 13 to 15 mm. in thickness.

Lungs.—The left lung is voluminous. The vessels and bronchi at the hilum are clear. The pleural surface shows the adhesions described above, some of which are invaded by delicate capillaries. On section the lung tissue is everywhere very moist and exudes a frothy serous material. It is of a yellowish-red tint in the upper lobe, becoming deeper red in the lower lobe. Here and there one sees a few slightly raised purplish areas of irregular size and extent, which are rather dryer than the surrounding tissue and just palpable. At the bifurcation of the main bronchus one finds a calcified lymph-gland, measuring 2 cm. in long diameter. In the apex of the upper lobe is found a small calcified nodule 3 to 4 mm. in diameter, above which the pleura shows fibrous tags. Further examination of this scarred apical portion shows two or three other small foci of cheesy material, none of them exceeding 5 mm. in diameter. The *right* lung shows a condition in general resembling the left. There are numerous subserous hæmorrhages over the lower lobe. Cut section resembles the other lung. It is very moist. The right lung is even more voluminous than the left.

Spleen weighs 375 gms., measures 18 by 9 by 4 cm. It is adherent by old adhesions to the diaphragm. Its capsule shows numerous irregular milky areas of thickening. On section the Malpighian bodies appear very conspicuously as large indefinite milky dots, 1 to 1½ mm. in diameter. The spleen pulp is of a brick-red color, and scrapes off with ease on the knife. The trabeculæ are easily seen. The organ is flabby and flattens out on the table.

Stomach is greatly distended with sour-smelling clotted material. Its mucosa shows considerable postmortem digestion and occasional ecchymoses. The duodenum shows a velvety mucosa, stained with bile. The bile papilla is normal. The bile and pancreatic ducts open side by side, they are delicate and normal everywhere.

Pancreas is rather large and pale. Consistency is about normal. Cut section shows a pale watery-gray parenchyma, on which one sees distinctly minute opacities of pin-point size. The stroma does not seem to be increased in amount, but is quite loose and œdematous.

Liver weighs 2570 gms., measures 29 by 24 by 9 cm. Its upper surface is covered over by moss-like elastic adhesions, some of which show invasion with blood-vessels. The lower surface shows a similar, but less extensive peritonitis. Cut section is everywhere quite uniform and pale. The lobulation is distinct, the lobules being rather swollen, with a pale-red center and a more opaque-gray periphery. Here and there are seen a few minute areas of yellowish opacity, one of which looks like a small tubercle. Consistency is about normal.

Kidneys weigh 420 gms. The left kidney measures 13 by 6 by 3½ cm. The capsule comes off easily, leaving a pale smooth surface, showing occasional retention cysts. Cut section shows a pale-gray cortex, averaging 6 to 7 mm. in thickness. The striations are perfectly regular. The majority of the glomeruli appear as minute red dots. The tubular portion of the cortex is swollen and gray. The pyramids are normal. The pelvis is normal. The right kidney resembles the left.

Adrenals are of normal size. On section show an opaque-yellow cortex, 1 mm. in diameter, and a thin brown medulla.

Thyroid appears normal; the neck organs could not be removed.

Aorta shows a few small patches of yellowish thickening. It retains its elasticity well.

Bladder shows a pale smooth mucosa.

Rectum normal.

Prostate, seminal vesicles, and *testicles* normal.

Marrow of femur is of a mottled yellowish-pink color and rather firm.

Intestine.—The jejunum is dilated, shows a pink or red velvety swollen mucosa, which is flecked over thickly with little pin-point yellowish grains, which seem to be intimately connected with the mucosa, even in some cases beneath it. No ulcerations are seen. The lower portion of the jejunum shows a rather paler mucosa of the same description, and everywhere thickly dotted over with these little yellowish-white grains. The Peyer's patches in the ileum are not conspicuous. The large intestine shows a pale smooth mucosa.

Mesenteric glands present a most remarkable appearance. They are greatly enlarged, some of them measuring 3 to 4 cm. in long diameter. They are rather elastic to the touch. There are many small glands close to the mesenteric attachment, about ½

cm. in diameter. On section the smaller glands are found to be of an opaque pale-yellowish color, with almost complete disappearance of the gland tissue. There is an indefinite translucent reticulum, through which one sees minute grains of opaque yellow color. These are thickly sown throughout all the glands, and in some instances seem to be located in cyst-like pockets, from which these little grains can be scraped out on the edge of the knife. Some of the larger glands present considerable injection and show some small hæmorrhages into this translucent stroma, which everywhere is dotted over with these little grains of yellowish color. The glands on section bulge beyond the capsules. A similar condition is seen in the glands at the root of the mesentery in the neighborhood of the pancreas. Some of the glands here measure 2 cm. in long diameter. Some of them are quite opaque and yellow. They seem to be full of little cystic areas, some of which contain a viscid fluid, others little yellow grains. The retroperitoneal lymph-glands about the cœliac axis show exactly the same picture.

Thoracic duct is dissected out. Smears made from its content and stained show no bacteria but many mononuclear leucocytes and large mastzellen. The fluid from the thoracic duct shows numerous small highly refractile droplets and small rosettes of pale greenish acicular crystals often attached to the side of a fat droplet.

Scrapings from the cut section of the mesenteric glands under the microscope show typical tufts and balls of delicate spindle-shaped crystals. These crystals dissolve with a slight amount of heat and are reformed on cooling. They come down in little star-like masses of needle crystals, which are much smaller than the original crystals. The crystals dissolve easily in alcohol and ether, and are evidently fatty acid. Similar crystals are found in the scrapings from the intestinal mucosa. Fresh cut section of the glands shows a neutral reaction to litmus. No bacteria are made out in smears. One of the small mesenteric lymph-glands is inoculated subcutaneously into a rabbit; animal died in seven weeks; negative for tuberculosis.

Microscopical Preparations.

Tissues hardened in Zenkers fluid, formalin, or alcohol. The routine stain was hæmatoxylin and eosin.

Heart.—The pericardial cavity is almost entirely replaced by a loose œdematous granulation tissue of connective tissue and wandering cells in which blood-vessels are quite conspicuous. There are numerous chinks in this granulation tissue which are lined by cubical epithelium derived evidently from that of the pericardial cavity. In some small areas there is an exudate of polymorphonuclear leucocytes, red blood-cells, and fibrin. The heart muscle-cells are of about normal size but show a moderate grade of fragmentation. The aortic valve shows a dense hyaline mass of old fibrin which is being invaded by fibroblasts, wandering cells, and blood-vessels.

Lungs.—The pleura is thickened and infiltrated with many wandering cells and new-formed blood-vessels. There are numerous adhesions consisting of scar tissue or organizing granulation tissue. Beneath the pleura many of the alveoli show an exudate of red blood-cells and heart-failure cells mixed in with a fine pink granular coagulum. Other alveoli show a hyaline-like exudate of fibrin which is being invaded by wandering cells, fibroblasts, and capillaries. In such areas the alveolar walls are greatly thickened, consisting mainly of a thick mass of young fibroblasts and blood-vessels. The alveolar epithelium here is cubical and beneath it are many phagocytes full of coarsely granular yellow pigment. In all sections of lung tissue the alveoli show some coagulated serous material and numerous heart-failure cells. In some areas the alveoli show a fresh exudate of fibrin, red blood-cells, and leucocytes. The bronchi in some instances show a similar exudate and the epithelium is well preserved. The capillaries are congested and the larger blood-vessels are normal. The lymphatic tissue of the lung is normal in amount and character. Coal pigment is present in moderate amount.

Spleen.—The capsule is thickened and shows signs of a chronic inflammatory process. The trabeculæ are thickened but widely separated from each other by an increase in spleen pulp. The blood-vessels show some thickening of their walls and in some instances a hyaline degeneration of the subintimal tissue. The Malpighian bodies are enlarged, but as a rule show no abnormalities. Some of them show an increase of stroma with disappearance of lymphoid-cells in the immediate neighborhood of the central arteriole and others show many polymorphonuclear leucocytes in their peripheral zone. The venules of the spleen pulp are full of blood and their walls are somewhat thickened, showing evidences of some chronic passive congestion. The pulp-cells are increased in number, between which are seen numerous cells of polyblastic type (Maximow), red blood-cells, and leucocytes. The stroma of the pulp is definitely thickened and easily made out. Numerous accumulations of coarsely granular yellow pigment are found in the pulp, often some of the smaller grains being included in large phagocytes.

Marrow of femur.—There is considerable increase in the cellular elements, but the fat-cells are quite in evidence making up more than half of any section and appear quite normal. The giant cells and myelocytes occur in normal proportion. The eosinophile cells are not increased in number. Red blood-cells are not conspicuous, but the nucleated reds are quite numerous and definitely increased in number. They occur in clumps of 3 to 20, which are scattered thickly throughout the sections. The same yellow pigment as described in the spleen is present in all parts of the cellular marrow and is often included in large phagocytes. The lymphatic tissue of the spleen and marrow shows none of the remarkable changes found in that of the mesentery and intestine, but the changes here are dependent on a secondary anæmia.

Blood-clots. Sections show no change of importance.

Liver.—The capsule is thickened and shows many adhesions made up of scar tissue and blood-vessels. The stroma at the margins of the lobules is increased in amount and invaded by many polymorphonuclear leucocytes which are present as well in the capillaries of the lobules. This change is most marked just beneath the capsule and seems to have a direct relation to the extensive perihepatitis. The capillaries in the central portion of the lobules are dilated with a corresponding atrophy of the liver cells which here contain fine yellow pigment. The liver cells at the margin of lobules are swollen and granular, some of them showing small fat vacuoles. The bile-ducts are perfectly normal.

Adrenals.—Its cortical cells are regularly arranged and of the usual appearance. Many of them show fat vacuoles. The medulla is inconspicuous. The perirenal fat is quite normal in appearance.

Kidneys.—The cortex shows a regular architecture, but there is a slight diffuse increase in connective tissue between the tubules. The glomeruli are of normal size, but many show some thickening of their capsules. The convoluted tubules show a swollen pink-staining granular epithelium which shows the "brush border" quite well and whose nuclei stain sharply. Their lumina are slightly dilated and contain foamy or granular-looking débris but no casts and no exudate of cells. The pyramids show normal tubules which contain no casts, but the interstitial stroma is quite œdematous. Blood-vessels are normal and the capillaries contain little blood.

Pancreas.—Sections from various parts of the organ show no changes of importance. The islands of Langerhans are rather large, sharply outlined by a thin capsule, and made up of normal-

looking cells, a few of which show mitotic figures. The acini in many places show postmortem changes, but elsewhere are normal, as are the pancreatic ducts. The interlobular stroma is loose, its meshes being separated by a pink granular coagulum in which can be made out a few mononuclear wandering cells. The fat-cells in this stroma are normal. The interacinar stroma is very delicate.

Skin and subcutaneous tissue from abdomen is quite normal. The fat-cells are sharply contoured.

Thyroid.—Its acini are regularly arranged and contain normal colloid. The interacinar stroma is loose and œdematous, showing as well some pale-staining colloid material.

Jejunum and ileum.—Sections made from various levels in the small intestine all show the same general picture.

Frozen sections stained lightly with osmic acid and Soudan III, show deposits of fat in the villi and submucosa. Fatty acid crystals are not stained and show up very clearly as rosettes of needles which are intimately associated with the neutral fat (compare Fig. 1) and make a beautiful contrast. Tissue hardened in formalin and stained by the Marchi method (1) shows the presence of large masses which reduce the osmic acid and are called fat droplets for the sake of brevity. The fat in the tissue at the mesenteric attachment stains as usual, appearing as large oval or circular, sharply and evenly contoured masses of a uniform jet black. Large black masses are seen in the interglandular tissue of the mucosa and in the submucosa (Fig. 2). These are not evenly contoured, but show nodular or even serrated margins and all manner of shapes. They do not stain uniformly and one may see the center or any portion of a large mass which has a feathery or fern-like appearance, due evidently, to the presence of the crystals of fatty acid. In some instances the outlines of typical rosettes are preserved in the Marchi preparations of the intestine, but this finding is common in the gland tissue. The crystals reduce the osmic acid, but they are not as black and opaque as the fat droplets. The majority of the black masses fill the spaces in which they lie but some only partly do so, the rest of the space being filled with a fine reticulum of coagulum suggesting lymph. Some of these spaces in the villi contain a fine spider-web-like reticulum of coagulated material in which may be embedded a few mononuclear cells or a small droplet of fat (Fig. 8). A lining endothelium can often be made out in such cases, suggesting that these are dilated lymph radicles perhaps occluded by a fat embolus located proximally. One may see droplets of varying size, many of which do not exceed twice the diameter of a lymphocyte, and they may be so closely packed that it seems sure that there is a deposit of this fatty substance *outside* of the lymphatics as well as in their lumina. The epithelial cells lining the crypts of Lieberkühn show no fat droplets, but there are many goblet cells with accumulations of mucus. They are quite normal in appearance. The interglandular stroma shows but few very fine grains of fat such as one finds in its venules in the circulating white corpuscles. A few of the large mononuclear cells of the plasma-cell type show these fine black grains, but the peculiar cells which are distinctly abnormal in this location do not show any fat grains, or at the most only a few. These cells have a vesicular nucleus and a pink-staining, frothy-looking protoplasm. With ordinary stains the cells seem to be packed with fine fat vacuoles of nearly uniform size, but these do not stain with osmic acid. The polynuclear giant cells are not numerous and show only occasional fat grains. The solitary follicles show no large accumulations of fat, but they are invaded by numbers of the large mononuclear cells. Some of the plasma cells here show a few grains of fat. The muscularis mucosæ is quite thickly sprinkled with fine black grains, which seem to be both intra- and extra-cellular. The capillaries and venules in this neighborhood often show some fatty grains in the endothelial cells.

Sections stained with hæmatoxylin and eosin show the very conspicuous vacuoles (Fig. 3), many of which contain a finely granular, pink-staining reticulum. Some of these vacuoles are lined by endothelial cells, giant polynuclear cells, numbers of the large mononuclear "foamy" cells, or a combination of any or all of them (Fig. 3). Other vacuoles are surrounded by a thin capsule of quite dense fibrous tissue in which are embedded many or few of the wandering cells. The interglandular tissue is made up of numbers of lymphocytes, plasma cells, and eosinophiles in about the normal number, plus the unusual mononuclear cells (Fig. 4). There seem to be two kinds of large mononuclear cells or very different types of the same cell. One resembles exactly the "polyblast" of Maximow (2) and is not very numerous here. Its protoplasm stains a deep pink and is finely granular, while its nucleus is vesicular, but shows well-marked strands and grains of chromatin. The majority of the giant cells appear to be formed by a fusion of such cells and show the same type of nucleus and protoplasm. The second type of cell has a pale vesicular nucleus, which is poor in chromatin, 5 to 7 μ in diameter and often eccentrically situated. Its protoplasm is abundant and has a foamy appearance, due to the presence of closely-placed vacuoles or granules which are often quite uniform in size, but may vary from 5 μ down to the size of an eosinophile granule. Some of the granules seem refractile and suggest mastzellen, but stains for these cells (1) show the same "foamy" protoplasm with non-staining vacuoles. Mastzellen are present in considerable numbers.

The "foamy" cells average 20 to 30 μ in diameter but show evidence of active motility and are of every conceivable form. Mitoses are seen in these cells very rarely. They are occasionally phagocytic to red blood-cells, old blood pigment or nuclear fragments. A few cells are seen which may be transition forms between them and the common polyblast, showing a vesicular nucleus and finely granular pink protoplasm, in which are a few of the vacuoles described in the "foamy" cells.

Maximow (2) describes cells ("eiterphagocyten") which in some points resemble these "foamy" cells, but his cells contain granules which stain by various methods. Such cells he considers to be derived from the mononuclear lymphocytes of the blood, as is true of the polyblasts. The "foamy" cells form giant cells either by fusion or nuclear division, the protoplasm retaining its peculiar appearance (Fig. 4). Some nuclei show signs of degeneration, but this is unusual, and the activity of the cells speaks against their being types of degenerating polyblasts.

They are most numerous in the tips of the villi and about the fat deposits where they often make up the entire field, with almost complete absence of the lymphocytes and plasma cells. As a result of all this invasion of foreign cells and fat deposits the villi are greatly increased (more than double) in length and diameter. Their capillaries are dilated, and the connective tissue is increased in amount. There is evidence of an occasional old or recent extravasation of red blood-cells into the villi, where one may see a few phagocytes packed with yellow granular pigment. Well-preserved red blood-cells may be seen free in the tissue round the bases of the crypts. A few polymorphonuclear leucocytes are seen in these areas. The solitary follicles are but slightly enlarged and the prevailing cell is the lymphocyte. Some are invaded by numbers of the "foamy" mononuclear cells but no very striking changes are seen.

The muscularis mucosæ shows hypertrophy. The *submucosa* in some places is almost normal, but as a rule is much thickened, its vessels dilated and thickened, and the stroma filled with wandering cells. The predominant mononuclear cell is the polyblast and they often contain fine grains of fat (Marchi). Many of the "foamy" mononuclears are present, usually in the loose stroma just below the muscularis mucosæ and in the neighborhood of fat deposits. The fat droplets in some places are so

closely placed as to suggest subcutaneous fat, but close inspection shows that they are of irregular size and shape. Their margins are often outlined by giant and mononuclear cells (Fig. 3) and they are separated from each other only by a delicate granulation tissue of fibroblasts, capillaries, and wandering cells. Again, the tissue will be dense and fibrous, containing only a few fat droplets and wandering cells. Numbers of extravasated red blood-cells are seen in the submucosa, often in large clumps, but usually diffusely scattered. Yellow granular blood pigment is frequently seen included in phagocytes and is most abundant in those areas where the fat deposits are most numerous. Large eosinophile mononuclears are quite numerous in all parts of the submucosa. Careful search with oil immersion lens in sections stained by various methods failed to reveal any bacteria or parasites which could have any relation to the lesion. The muscle coats and the ganglia of the plexuses are normal. The ganglion cells show some fine fat grains in their protoplasm. The serous coat shows an organizing granulation tissue of wandering cells, capillaries, etc., of the usual type.

Glands.

Unstained frozen sections show refractile fat globules and great numbers of long acicular fatty acid crystals arranged in sheaves and rosettes. Stained lightly with osmic acid such sections give a picture represented in Fig. 1, which shows well the large and small droplets thickly sown through the gland tissue and a rosette of crystals. Marchi preparations show even more extensive fatty deposits (Fig. 5) than were seen in the intestine. The gland deposits are larger, even more irregular and closely packed, but in general closely resemble those described above. In places the fat is deposited in threads which are twisted, beaded, and packed together, resembling a reconstruction of the glomerular capillaries. Such deposits are often seen in a follicle and no endothelial cells can be made out in relation to them. Giant cells are numerous and closely applied to the margins of these fat deposits, often in little lacunæ as though they were ingesting and eroding its substance. These cells may show a fine granular protoplasm and a few fat droplets; other giant cells in the stroma may show clumps of small fat droplets in their protoplasm which may have the "foamy" appearance. Some of the giant and mononuclear cells with the foamy protoplasm show minute comma-shaped black deposits which often outline one segment of a vacuole in the protoplasm, others are rod-shaped, again beaded like small filaments of chromatin, but always in the protoplasm. Often they are associated with definite grains of jet black fat deposits in the protoplasm and for this reason are thought to be some form of fat. The wandering mononuclear cells show varying amounts of fat deposits, some only a few minute grains, others large clumps of large and small droplets, and some are so crowded with fat droplets that the protoplasm and nucleus may be almost obscured. Cells with the foamy protoplasm seem less actively phagocytic toward the fat, and great numbers of them are entirely free from it. Just beneath the thickened capsules of some of the larger glands is seen a fine cloud of minute fat droplets (Fig. 5) which are very thickly packed all through the rather œdematous stroma. Some of these grains are intra-cellular, but many are surely extra-cellular. In such areas the large foamy mononuclears may be very numerous and yet show almost no phagocytosis of fat. It is possible that this material has recently reached the cortex of the gland from the afferent lymphatics. Some of the larger lymphatics at the hila of glands (efferent) are filled with a fine granular coagulum of albuminous material in which may be seen scattered small fat granules. The fat cells of the mesenteric tissues adjacent to the gland capsule are sharply contoured by thin cell membranes and look entirely normal except for some infiltration of the intercellular tissue by small round cells, chiefly lymphocytes and plasma cells. Sections of various glands stained with hæmatoxylin and eosin show how extensive is the change in the larger glands. The tissue is honey-combed with the fat vacuoles and much of the cellular structure is replaced by dense fibrous tissue which is poor in cells (Fig. 6). It takes a deep blue stain with Mallory's connective-tissue stain. The capsule and trabeculæ are thickened and the blood-vessels dilated and increased in number.

Some of the small glands which are slightly involved show almost normal lymphatic follicles and cords, but the peripheral lymphatic sinus may be greatly dilated by an exudate of red blood-cells, mononuclear wandering cells, a few polymorphonuclear leucocytes and lymphocytes, mixed with a finely granular pink coagulum. There are small irregular fat deposits which usually first appear in the medulla of the gland between the intact lymph-cords. They are outlined roughly by collections of giant and mononuclear cells, but endothelial cells are rarely made out. The adjacent tissue is at once invaded by numbers of large mononuclear cells, eosinophiles, young fibroblasts, and capillaries forming a loose cellular granular tissue about the deposits. It is quite possible that this cellular reaction may preceed the fat deposits. This granulation tissue gradually becomes dense and fibrous causing the great distortion of the gland architecture seen in several of the photographs (Figs. 6 and 7). Free red blood-cells are present in great numbers in both large and small glands, but the ecchymoses are more striking in the older glands. Phagocytosis of red cells by polyblasts is present, but not conspicuous, and is relatively infrequent when we consider the number of both types of cells. Changed blood-pigment included in phagocytes or chinks of the stroma is hard to find except in the larger glands. In some of the small glands the eosinophile cells are very definitely increased in number, mononuclears predominating, and suggest the presence of some parasite.

A small gland which was preserved in 15 *per cent formalin and stained by the Levaditi method, showed some very peculiar structures. Studied with* 1/12 *objective these sections show great numbers of a rod-shaped organism* (?) *which, with this stain, is about the diameter of the spirochæte of syphilis but not of spiral shape and rarely exceeding* 2 μ *in length. The majority of these structures closely resemble in form the tubercle bacillus. They are very sharply contoured and appear as jet black rods, sometimes bent but more often straight or only slightly curved. Some show a slight swelling of one end and others a beaded appearance. They are most numerous in the vacuoles, which are not completely filled with fat and contain a filmy granular reticulum* (*Fig.* 9). *The structures are most numerous at the edge of the vacuoles, where the "foamy" cells are in evidence, and are contained in great numbers in these cells. When a cell contains very many of these structures they seem to clump together and lose their sharp outline as though damaged by the process of ingestion. These structures are present at the edge of the fat droplets in less numbers and become less numerous in the adjacent tissue. Careful search made in corresponding sections stained by various aniline dyes reveals no corresponding structures. If we compare them with the various spirochætes which take this stain we, perhaps, may imagine that we are dealing with some organism which resists the common stains but reduces the silver salts, effecting considerable increase in its size. Whether this is the active agent in this peculiar pathological complex cannot be determined from the study of this single case, but its distribution in the glands is very suggestive. No tissue from the intestines nor viscera was available for the Levaditi stain and all the smears from the thoracic duct and glands were used before the study of the glands by the silver method revealed these peculiar bodies.*

The vacuoles do not all contain fat deposits, some of them (Fig. 8) showing only a delicate tracery of granular pink coagulum. In such spaces there may be a few degenerated cells or

small fat droplets or the coagulum may show an exact mould of a rosette of fat crystals which have been dissolved. Some of the smaller glands have a very œdematous stroma, and all the cellular elements are widely separated. Here the large mononuclear cells show many degeneration forms in which the protoplasm is full of very large irregular vacuoles and the nucleus very faint or even non-staining. In all sections many areas are found where there are large accumulations of the large foamy or granular mononuclears and here the degeneration forms are often conspicuous. Mastzellen are present in all sections, but not numerous. One large giant cell with pink granular protoplasm is seen in mitosis, the chromatin threads being very coarse and arranged as though the division was to result in three or four cells.

Briefly the microscopical findings in the intestinal and mesenteric lesions may be summarized as follows: The villi of the small intestine are enlarged, the submucosa thickened, and the mesenteric glands enormously enlarged by deposits of osmic acid reducing bodies (neutral fats and fatty acids). Such deposits are most numerous in the glands, but alike in all these situations. They are of all sizes from minute grains intra- or extra-cellular in location, up to huge irregular droplets and there is the greatest variety of forms (Fig. 2 and 5). Many of the larger masses show rosettes of fatty acid crystals (Fig. 1) and they may occupy spaces which are lined by endothelium suggesting dilated lymph channels (Figs. 6 and 7). The majority of the larger deposits are outlined by polynuclear giant cells or large mononuclear cells of polyblastic type which in some instances seem to be eroding the fatty material and are closely applied to its edge. (Fig. 8). The epithelium of the *mucosa* is normal as far as the microscope shows. The interglandular stroma contains about the usual number of lymphocytes, plasma cells, and eosinophiles, but there is an infiltration with great numbers of polyblasts—large mononuclear, ameboid cells with pink granular protoplasm. A second type of cell which is very conspicuous has an abundant foamy protoplasm, a pale vesicular nucleus and is actively ameboid; this may be a type of polyblast. Ecchymoses are numerous wherever we find the fatty deposits. The *submucosa* shows invasion with great numbers of these polyblastic cells especially about the fat deposits which in some places are abundant (Fig. 2); in others absent. There may be a very definite eosinophilia in such areas. The *glands* show the most extensive changes, especially the larger ones (Fig. 6-7). In some the lymphatic nodules and cords are quite intact, the process seeming to begin in the sinuses of the glands with invasion of the characteristic cells and small irregular fat deposits. The next stage is an invasion by fibroblasts and capillaries with more or less extravasation of blood, increase in size and number of the fat deposits and distortion of the gland architecture (Fig. 8). The large mononuclear cells increase rapidly in numbers and giant cells become conspicuous. The final stage shows a very large gland packed with fat deposits of all sizes and shapes, whose stroma is made up of dense fibrous tissue full of ecchymoses and great numbers of giant and mononuclear cells (Fig. 6-7). Gland tissue treated by the Levaditi method shows great numbers of a peculiar rod-shaped organism (?) which does not stain by the aniline dyes and is most numerous in the vacuoles and in the neighborhood of the peculiar "foamy" cells which often include these structures (Fig. 9). Whether this is the etiological factor in this disease can not be determined from this case.

BACTERIOLOGY.

A bacillus belonging to the colon group was isolated from the mesenteric glands. Cultures from the parenchymatous organs showed a white coccus of low virulence.

A small gland was planted subcutaneously in a large gray rabbit. The animal died of pneumonia seven weeks after the inoculation. Autopsy showed a small subcutaneous abscess full of soft yellow pus. The glands draining this area were only slightly enlarged. Microscopical sections show an abscess wall of granulation tissue containing many large mononuclear phagocytes closely resembling those described in the human tissue. The central part shows necrosis. Gland-tissue from the axillæ shows merely a moderate grade of chronic inflammation and there is no evidence of tuberculosis.

CHEMISTRY.

The microscopical picture was so suggestive of an abnormal fat or a mixture of fats, fatty acids, and perhaps some toxic substance which resisted absorption by the surrounding granulation tissue that a chemical study of the glandular tissue was attempted. The small amount of available material did not permit of extended chemical investigation, but the following facts are clearly brought out. 1. The ratio of fat to fatty acid. 2. The saponification value. 3. Several negative qualitative tests.

Liver, spleen, kidney, and small intestine.—About 10 to 15 gms. of each organ were ground up in about 50 cc. of 95 per cent alcohol and allowed to stand in bottles for several days. The tissues were extracted and tested for fatty acid which was found to be present in traces in the first three tissues, and to a greater degree in the intestine. Neutral fat was present in all, apparently in normal amount.

Mesenteric glands.—About 3 gms. of material (a single large gland) preserved in 95 per cent alcohol was extracted in the Soxhlet apparatus for six hours, the alcoholic and ether extracts united and evaporated to an oily residue. Glycerine was tested for and shown to be absent. The oily residue was made alkaline and the fat removed by repeated extractions with ether. The alkaline solution showed a typical soapy appearance. This was shown to contain a soap by the following reactions: 1. One portion acidified with hydrochloric acid gave a precipitate which was soluble in alcohol. 2. A second portion treated with calcium chloride gave a typical precipitate of calcium soap which was insoluble in alcohol. The solution was made acid and the fatty acid removed with ether. The ether was evaporated and the residue weighed. The neutral fat extracted by this method weighed 0.75 gms. and the fatty acid 0.07 gms., giving a ratio of 10 to 1.

A second determination was made by another method. Four medium-sized glands weighing about 4 gms. were cut open and preserved for three weeks in about 50 cc. of 80 per cent alcohol. This alcohol was filtered off and evaporated over the water bath to a dark brown oily residue—1st fraction. The glands were then ground up thoroughly with sand and absolute alcohol and the alcohol filtered off. The residue of tissue macerated with the sand was extracted in the Soxhlet apparatus for 24 hours with ether and the ether and alcohol extracts combined. This

was evaporated on the water bath to a white waxy material—2d fraction. The glands were further extracted in the Soxhlet for a second 24 hours, but this ether extract on evaporation gave only a trace of fatty material—3d fraction.

Material from the 1st fraction (0.1116 gms.) was dissolved in neutral 80 per cent alcohol and titrated against a known solution of alcoholic potash (7.8873 gms. per liter). It required 1.05 cc. of the alcoholic potash solution to neutralize the free acid. Then 8 cc. of the alcoholic potash were added and the solution heated over a water bath with return condenser for one hour to saponify the neutral fat. At the end of this time the solution was a deep cherry red showing an excess of alkali was still present. It was found that 2.58 cc. of the alcoholic potash had been used up by the fatty acids which were set free in the saponification. This gives an approximate ratio of 5 to 2 for the fats and fatty acids in the 1st fraction. Material taken from the 2d fraction (0.198 gms.) was treated in an identical manner. This solution required but 0.35 cc. of alcoholic potash to neutralize the free fatty acid, but 3.69 cc. were used up during the saponification. This fraction showed a much higher percentage of neutral fat, the ratio to fatty acid being roughly 10 to 1. The saponification number of this material from the 2d fraction as determined by Dr. Loevenhart was 144.4. When the weights of the 1st and 2d fractions were combined the ratio of fats to fatty acids was found to be about 85 to 15 per cent—1.552 gms. fat and 0.234 gms. fatty acid extracted from all the tissue. Tests for bile pigments were negative. Tests for phosphorous were made as follows and shown to be negative. Material from the 1st and 2d fractions boiled 5 to 10 minutes with potash, then acidified with nitric acid and an equal amount of ammonium molybdate added. On boiling this solution no yellow precipitate was obtained, but the addition of one drop of an acid sodium phosphate solution gave the yellow precipitate in abundance. This test excludes the presence of lecithin in any appreciable amount. The 1st fraction showed many crystals of various types. Some of these were needles of fatty acid and others chlorides or phosphates. No crystals of cholesterine were seen. The 3d fraction showed a few tufts of beautiful slender acicular fatty acid crystals.

It is unfortunate that the tissue was not sufficiently fresh to test for enzyme action (lipase), but the following facts are suggestive. Fatty acids (0.23 gms.) were present in these abnormal mesenteric glands and presumably the majority of them were derived from high melting point fats because the well-formed crystals were present in large numbers even with a room temperature of 32 C. Neutral fats were present (1.55 gms.) and showed a low saponification number (144.4) which indicates either some abnormality of the fat or the presence of some non-saponifiable substance mixed with it. Lecithin and cholesterine were suspected but shown to be absent. In the determination of the saponification number no allowance was made for the included fatty acid (10 per cent) which would tend to raise rather than lower the number, making the contrast with normal fats somewhat less striking but would in all probability leave it abnormally low. The saponification numbers of the common fats are tripalmitin = 208.8, tristerin = 189.1, triolein = 190.4, horse fat = 199.4, hog fat = 195.6.

Discussion.

Many features of this case were of great interest but it seems that in the light of our present knowledge a lengthy discussion would be of little value. The finding of acetone in the urine shortly before death and the extreme air hunger at this time suggested some acidosis which may have been dependent on the disturbance in fat metabolism. However the acetone could be accounted for by the starvation of the tissues following the obstruction of the mesenteric lymphatics and we know that in spite of heavy feeding the patient was steadily losing weight. The large amount of unsplit fat in the stools (one-half by weight) may be explained by the incomplete action of the lipolytic ferment owing to lack of absorption of its split products. Again there may have been some lack of lipase in the pancreatic secretion, but the normal appearance of the gland is opposed to this view. The deposits of neutral fat and fatty acids in the tissues may indicate some disturbance in the synthesis of fat which Loevenhart (3) and others (4, 5) have shown to be effected by lipase. Several facts indicate that this fat is in itself in some way abnormal or that it holds in suspension some abnormal or toxic substance. 1. The saponification number is very low. 2. The fat causes a tissue reaction resembling the reaction due to an inert foreign-body. 3. The peculiar wandering and phagocytic mononuclear cells. 4. The presence of many minute ecchymoses and changed blood pigment suggests some toxin capable of effecting the solution of the capillary walls. The pathological changes are limited to the apparatus which has to do with the absorption of fats while the lymphatic tissue of the marrow, spleen, bronchial glands, etc., is relatively normal except for the changes consecutive upon a rapidly advancing secondary anæmia, resembling that seen in cancer cachexia. All this suggests very strongly that here we are dealing with some obscure disease of fat metabolism.

The disease is of some duration as evidenced by the extreme changes in some of the larger glands which show dense scar tissue and cellular reaction which must be of months' standing. From a comparison with the intestinal lesions it would seem probable that the earliest changes took place in the glands rather than in the mucosa where the dense scar tissue is much less in evidence although in general the picture is the same. Examination of the contents of the thoracic duct excludes the possibility of any occlusion of its radicles between the glands and receptaculum. The presence of fatty acid crystals in its contents must be explained by the escape of such material from the glands and the same explanation holds for the mastzellen. The presence of many eosinophile cells in the smaller glands probably accounts for the same type of cell found clinically in the blood, but no clear explanation has been found for this reaction.

The presence of peculiar structures in the Levaditi sections which do not stain by the aniline dyes, suggests a possible relation to the group of spirochætes. It is not claimed that this is the etiological factor in this disease but its distribution in the glands is very suggestive. It is always found in the peculiar vacuoles and cellular granulation tissue which are the striking features of the microscopical picture in the glands and intestine.

There seems no sufficient reason to correlate the intestinal,

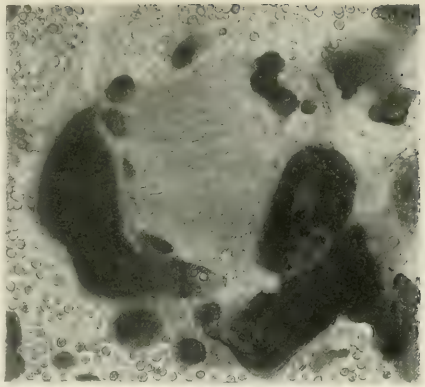


FIG. 1.—Frozen section of small mesenteric gland stained lightly with osmic acid. Rosette of fatty acid crystals and deposits of fat among lymphocytes.

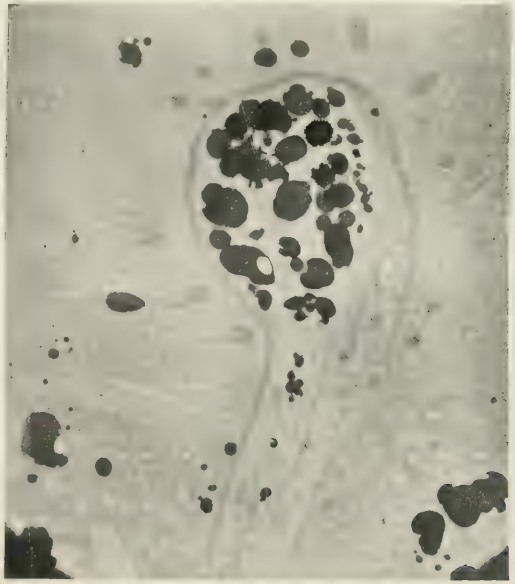


FIG. 2.—Marchi preparation. Cross section of one of the circular valves of the jejunum. Large central deposit of fat in the submucosa and on either side deposits in the mucosa. Solitary follicle (*a*).

FIG. 3.—Fat vacuoles (*a*) in mucosa and submucosa. Giant cell (*b*). Large mononuclear "foamy" cells (*c*).

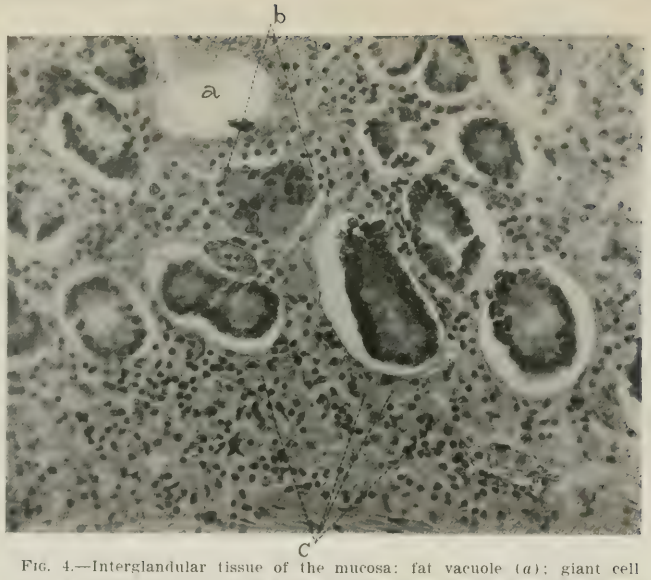


FIG. 4.—Interglandular tissue of the mucosa: fat vacuole (*a*); giant cell (*b*), and "foamy" cells (*c*). The muscularis mucosæ just appears at the base.

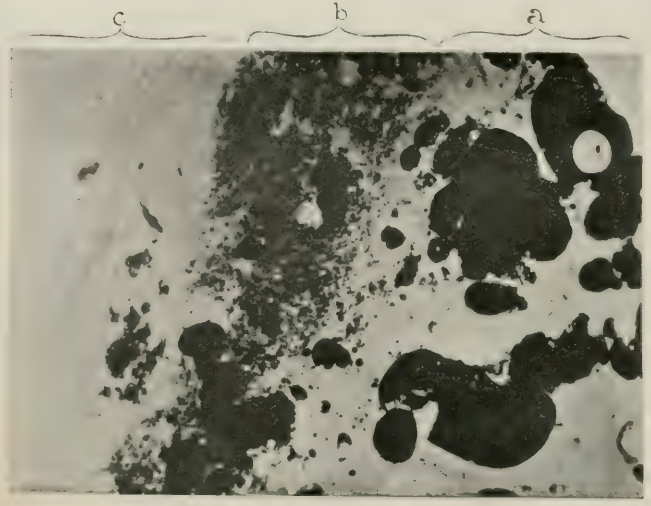


FIG. 5.—Marchi preparation. Cortex of large mesenteric gland. Large fat droplets (*a*); fine thickly placed fat droplets (*b*), and thick gland capsule free from fat (*c*).

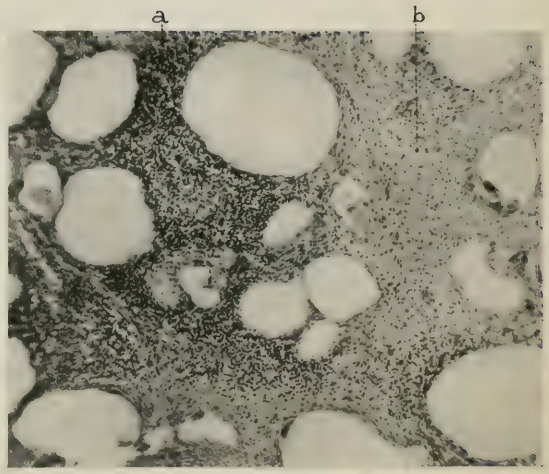


FIG. 6.—Large gland full of dense scar tissue (*b*); fat vacuoles lined with endothelium or giant cells. Normal lymphatic cells (*a*).

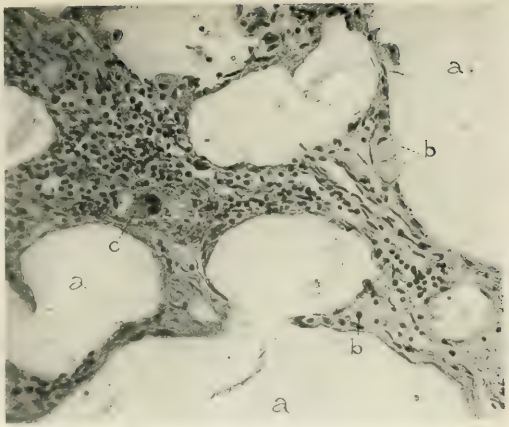


FIG. 7.—Large gland with thickly packed fat vacuoles (*a*); "foamy" cells at edge of fat deposit and in stroma (*b*); giant cell (*c*).

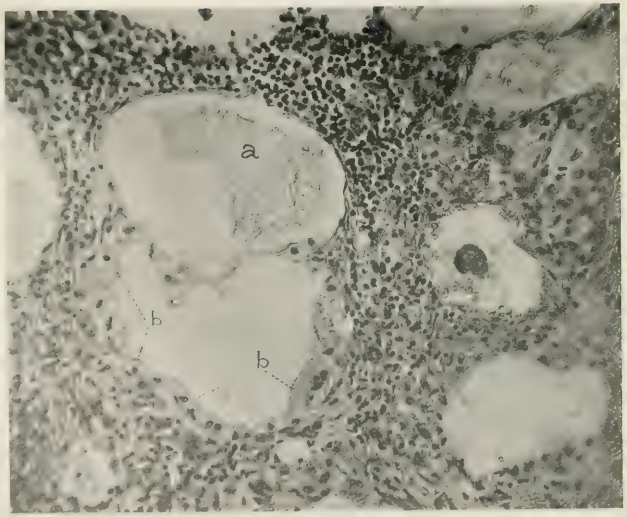


FIG. 8.—Small gland with more recent changes; red blood cells scattered through the tissues. Vacuole (*a*) contains a filmy granular coagulum. Rim of "foamy" poly- and mononuclear cells (*b*) at edge of fat deposit.

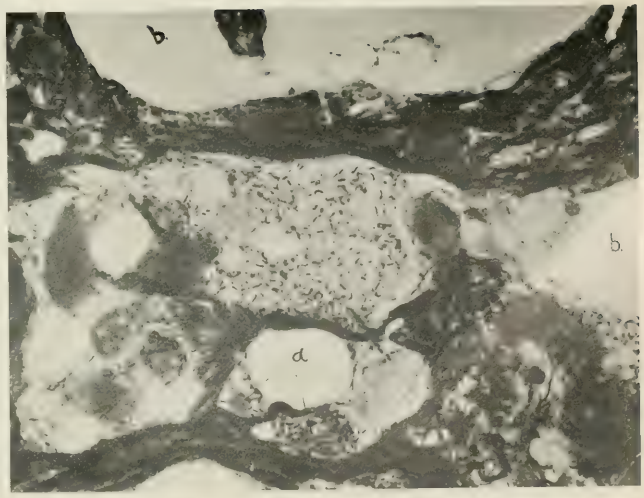


FIG. 9.—Section of gland stained by Levaditi method. Vacuole (*a*) containing rod-shaped organism (?).

arthritic, and serous lesions but it is possible that the organizing inflammatory reaction affecting the pleura, peritoneum, and aortic valve may be closely related to the peculiar arthritis and purpura which we were unable to examine at autopsy.

In searching for a name to designate this condition great difficulties were encountered. It would seem that no suitable name can be applied to it until the etiological factor is determined. The term *Intestinal Lipodystrophy* is suggested as this seems to offer less objections and to have more points in its favor than any one word or combination of words which have been considered.

In conclusion I wish to express by most sincere thanks to Dr. Thayer for his careful clinical analysis of the case which was under his care in the private wards, to Dr. Loevenhart for valuable assistance in the chemical study of the tissues, to Dr. Voegtlin for analyses of the stools and urine, to Dr. Ford and Mr. Harrison for the bacteriological examinations, to Dr. Welch and Dr. MacCallum for their interest and valuable suggestions, to Mr. Brödel and Mr. Ridges for assistance in preparing the illustrations.

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PANCREATITIS AND FOCAL NECROSES.

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In the following communication an attempt is made to show that the pancreas often presents minute focal necroses which at times may be related to fat necrosis and acute hæmorrhagic pancreatitis, as well as to some types of chronic diffuse pancreatitis. In the last 300 autopsies at the Johns Hopkins Hospital a careful study has been made of the pancreatic glands in 230 cases. The bile and pancreatic ducts were examined carefully. In many cases tissue was studied microscopically from the head, body and tail of the organ. When a single piece of tissue was examined it was usually removed from the tail. These cases may be grouped and classified as follows:

Focal Necroses—41 Cases.

This group does not include the cases in the next three groups although many of them do show focal necroses. At times only a few very small necroses were found after long search, again many were found in a single lobule. Lobar pneumonia seemed to be the most active etiological factor, 11 cases; septicæmia, 6 cases; acute peritonitis, 6 cases; typhoid, 4 cases; bronchopneumonia (organizing), 3 cases; organizing endocarditis, 3 cases. The remaining cases were scattered (bronchiectasis, meningitis, collitis, hepatic cirrhosis).

The term "focal necrosis" is used to designate a type of focal degeneration affecting the pancreatic acini. The lesion usually appears as a granular change in the acinar epithelium with solution of the nuclei and rapid disintegration of the protoplasm. This change usually causes some increase in size of the affected acinus, and there is a very rapid invasion of polymorphonuclear leucocytes. In fact this change is recognized by the infiltration of leucocytes which may take place before the nuclei have vanished, although staining faintly (Fig. 1.). The basement membrane is quite resistant and as a rule remains intact even after all the acinar cells have undergone a granular degeneration and the membrane may only surround a granular detritus invaded by numbers of polymorphonuclear leucocytes. This change often affects acini which are dilated by pink colloid like casts and the colloid material may persist and be invaded by leucocytes after the acinar epithelium has been destroyed. These necroses as a rule are quite diffusely scattered through the parenchyma of the pancreas and quite small, commonly affecting but a single acinus or a part of one acinus. One may see a small segment of an acinus which shows a granular degeneration of its epithelium with invasion of 2 to 10 polymorphonuclear leucocytes in this tissue and in the lumen of the acinus. Frequently the necrosis will partially destroy the epithelium of 2 to 4 acini and there will be an invasion of leucocytes into their lumina and in the œdematous stroma between them. It is remarkable what a powerful attraction the degenerated acinar epithelium seems to have for the polymorphonuclear leucocyte. These small foci are soon invaded by mononuclear wandering cells (polyblasts) and fibroblasts, but usually a few polymorphonuclear leucocytes can be seen. 3 cases of organizing bronchopneumonia showed the changes just described, which appeared to be of about the same age as the pulmonary lesion but fresh foci were present as well. These small foci of degeneration which may contain many polymorphonuclear leucocytes do *not* as a rule contain bacteria. In a few of the cases of septicæmia where the necrosis involved several acini, clumps of bacteria could be demonstrated, but in not a single case of pneumonia with focal necroses could the organisms be demonstrated as having any regular relation to the degenerated tissue.

There is no regular association of pancreatic and liver necroses. In this series liver necroses were quite common in association with acute peritonitis. 23 cases of acute or organizing peritonitis showed liver necroses in 10, and pancreatic necroses in 6. 17 cases of lobar pneumonia: 8 showed no pancreatic necroses and 2 of these showed liver necroses; 9

showed pancreatic necroses and 2 of these showed liver necroses. Two of the cases showing thickly sown necroses in the pancreatic tissue, some of them involving 2 to 15 acini showed no liver necroses. 6 cases of septicæmia showed no pancreatic necroses. The term septicæmia as used here indicates cases in which antemortem cultures showed the presence of some organism in the blood or in which fresh and abundant cardiac vegetations were present. Liver necroses were found in 13 cases which showed no pancreatic necroses (pneumonia, typhoid, septicæmia, etc.).

Acute Diffuse Pancreatitis—6 Cases.

This group does not include cases which show any fat necroses, but only those cases presenting a diffuse inflammation of the parenchyma with numerous focal necroses in the acini and a diffuse infiltration of the damaged acini and œdematous stroma with many polymorphonuclear leucocytes (Fig. 2.). The older cases show invasion by polyblasts and fibroblasts, and a beginning organization. With a little experience these cases can be recognized at the autopsy if there is no advanced postmortem change. The organ is very pale and firm, sometimes almost of stony hardness. The ducts are clear and their walls thin. The lobules are large but clean cut and the parenchyma has a uniform semi-translucent watery gray color. It seems worth while to give a brief summary of these cases.

J. T. Colored male, 22 years. (Autopsy, 2700.)

Anatomical diagnosis.—Pseudo-lobar organizing pneumonia of both lungs; acute fibrinous pleuritis; acute bronchitis and lymphadenitis; focal necroses of liver; subacute pancreatitis; cloudy swelling of viscera.

Pancreas is large and extremely firm. The lobules are large and cleanly marked out. The parenchyma is semi-translucent, gray in color. The islands are visible as minute opaque pinpoint dots. Ducts quite normal. Bile ducts are clear throughout.

Microscopical study.—Sections from the head, body, and tail all show the same picture. There is a moderate amount of chronic diffuse increase in the stroma which is everywhere very œdematous and shows many wandering leucocytes and polyblasts (Fig. 2). In places there are young fibroblasts in the stroma. The acini show a focal granular degeneration with pale or non-staining nuclei, invasion by polymorphonuclear leucocytes as described in the scattered "focal necroses." Mitoses are present in some of the partially damaged acini. Many of the acini show dilatation of their lumina by deep pink staining colloid casts of various sizes. The interlobular stroma is not involved by the change which affected uniformly the delicate interacinar stroma. The ducts show no abnormalities. In places there is evidence of attempted repair by a loose granulation tissue of fibroblasts and polyblasts replacing 2 to 10 acini. Careful search for bacteria in sections revealed no organisms. Cultures from the lungs showed Micrococcus albus and aureus. 3 other cases showed an exactly similar picture: (1) Typhoid fever and peritonitis; (2) rapid pulmonary tuberculosis and bronchiectasis; (3) organizing bronchopneumonia and acute myositis. They all showed some grade of chronic cirrhosis as did the first case, liver necroses and a pancreas as described. 2 cases showed definite hyaline necroses of single acini or small clumps of acini, as well as the usual type of cell degeneration and solution. Ducts normal. No bacteria could be demonstrated in sections. 2 other cases showed in general the same picture, but bacteria were present in the sections. (1) Carcinoma of hepatic ducts involving the head of pancreas; jaundice; liver necroses. The pancreatic ducts were somewhat thickened, but not much dilated and not infected. There was a moderate degree of diffuse cirrhosis. (2) Acute leukæmia; acute nephritis, enteritis, and endocarditis. Ducts normal. There was no chronic cirrhosis of the pancreas, but merely the diffuse inflammation and scattered necroses. Bacteria could be demonstrated in some sections, but not in large numbers. The islands were normal in all this group of cases.

In all of these 6 cases we are dealing with a severe grade of toxemia as evidenced by the finding of liver necroses in 5, and pancreatic necroses in all. It seems probable that this very diffuse cellular reaction, in which the polymorphonuclear leucocytes predominate, follows some damage to the acinar epithelium. The following case makes a striking contrast to the preceding cases: (Autopsy, 2768) Chronic nephritis; acute general peritonitis. The pancreas shows an invasion of its interlobar stroma by a direct extension from the peritoneal inflammation. The interacinar stroma is only invaded slightly at the edges of the lobules and there are no necroses in the acini. Bacteria can be demonstrated in the œdematous interlobar stroma which is full of leucocytes.

These cases were all under careful observation in the wards of the Johns Hopkins Hospital, and gave no symptoms of pancreatic disease; and we may suppose this to be a reaction against some damage to the parenchyma by bacteria or their toxins, closely allied to the changes seen in some forms of acute nephritis. If the patients recovered such changes would surely go on to a chronic cirrhosis of the organ.

Fat Necroses—5 Cases.

These cases all show fat necroses in the pancreatic or peripancreatic tissues with no evident hæmorrhage. A brief summary follows:

(1) A. S. White female, 42 years. (Autopsy, 2710.)

Anatomical diagnosis.—Chronic pelvic peritonitis; stricture of rectum; operation and resection of rectum; fecal and urinary fistulæ; acute cystitis; double hydronephrosis; thrombosis of iliac and sacral veins.

Pancreas is very firm and rather small. Some areas are seen where there has been atrophy of parenchyma and replacement by greenish or gray semi-translucent tissue. In places the lobules are clean cut and easily separated from each other. No fat necroses seen in gross.

Microscopical sections from head, body, and tail show exactly the same picture as described in Autopsy 2700 (acute diffuse pancreatitis), but in addition the section from the tail shows three small typical fat necroses. These necroses are at the edge of lobules and not larger than 5 to 15 acini; they are surrounded by a halo of leucocytes and contain some bacteria as seen in sections. The tissue everywhere shows a diffuse pancreatitis with scattered focal degenerations or necroses. There is a slight grade of chronic diffuse cirrhosis. Ducts and islands are quite normal. Cultures from the viscera were sterile.

(2) S. White female, 23 years. (Autopsy, 2859.)

Anatomical diagnosis.—Chronic mitral endocarditis with stenosis; cardiac dilatation and hypertrophy; chronic passive congestion of viscera; cardiac thrombi; infarcts of lungs and kidneys; chronic diffuse pancreatitis with fat necroses; purpura.

Pancreas is enlarged and feels very firm and elastic. Cut section shows a pale grayish parenchyma on which the islands are quite conspicuous as minute opaque dots. The lobules are glued

together and vary greatly in size and shape. The head of the pancreas shows a most interesting condition. Scattered through this portion of the organ are numerous areas of opaque yellow color, not exceeding 1 mm. in diameter, oftentimes surrounded by a thin zone of hæmorrhage. Many of them are of typical chalky appearance. This change seems to be limited to the area supplied by Santorini's duct. The papilla of this duct appears to be normal. Its lumen is not dilated and it contains the usual slimy pale material. There are no hæmorrhages anywhere in the mucosa of this duct. The main duct opens into the papilla and is normal throughout in size and distribution. The vessels in this area appear normal. The lymph glands close to this area and along the body of the pancreas are of a deep purple color, but uniform on section. No necroses are seen.

Microscopical sections from various parts of the pancreas show the fat necroses to be localized in the head of the organ. They are situated at the edges of the lobules, of small size and outlined by leucocytes as a rule. Some of them show halos of fibroblasts and large mononuclear wandering cells (polyblasts). There is a very little blood pigment or fresh blood cells in some of these areas. The parenchyma everywhere shows a moderate grade of diffuse cirrhosis and extreme congestion of all its capillaries. The ducts and islands are normal. Numerous small focal necroses are present throughout all the sections and some of them show beginning organization. There is no acute diffuse inflammation. The distribution of these fat necroses suggests some agency of the duct of Santorini which may have been obstructed or infected, although there was no evidence of such changes.

(3) White female, 75 years. (B. V., 1907; autopsy, 82.)

Anatomical diagnosis.—Carcinoma of common duct; extreme icterus; extreme dilatation of hepatic ducts; liver necroses; chronic diffuse pancreatitis with fat necrosis; emaciation.

Pancreas very large, firm and pale. Ducts slightly dilated but smooth and patent. There is no obstruction at the papilla. There is glueing together of the lobules. One small area (2 mm. in diameter) is found in the tail which is of an opaque yellowish color and rather chalky appearance, suggesting a fat necrosis. No other necroses are found after careful search.

Microscopical sections from various parts of the pancreas show an extreme grade of chronic diffuse cirrhosis. One fat necrosis of the usual type is seen outlined by polymorphonuclear leucocytes. All sections show scattered focal necroses involving ½ to 5 acini and some show invasion by fibroblasts. The ducts are thick, but lined by normal epithelium. No hæmorrhages are present.

(4) W. A. B. White male, 56 years. (Autopsy, 925.)

Anatomical diagnosis.—Biliary cirrhosis of liver; icterus; ascites; chronic nephritis; bronchopneumonia; chronic pancreatitis with fat necroses.

Pancreas is large, gray, and firm. Just beneath the capsule are several whitish areas, the largest not over 5 x 1 x 1 mm. Numerous similar foci are found in the parenchyma on section, and they contain putty-like material. Bile ducts are quite patent.

Microscopical section shows a moderate grade of diffuse chronic cirrhosis. The ducts and islands are normal. Numerous fat necroses are seen at the edges of lobules, but no hæmorrhages. Focal necroses, some of which are organizing, are quite numerous in all the lobules. They are of small size, as a rule.

(5) A. F. White female, 72 years. (Autopsy, 2545.)

Anatomical diagnosis.—Carcinoma of bile papilla; icterus; dilatation of bile ducts; cholelithiasis; dilatation of pancreatic duct; pancreatic fat necroses; liver necroses.

Pancreas.—The head is very hard. A probe passed into the mass in the duodenum goes into the pancreatic duct which is enlarged, measuring 23 mm. in circumference. On opening this orifice it is found to be surrounded by a collar of opaque grayish white tissue exactly similar to that round the orifice of the common bile duct. This new growth seems to extend irregularly into the underlying pancreatic tissue. The distal portion of the pancreatic duct is enormously dilated and very tortuous. Its lining presents a peculiar beaded appearance. The pancreas on section is smooth and hard. It contains several cyst-like structures probably the result of retention. There is considerable infiltration with adipose tissue which here and there shows small chalky fat necroses.

Microscopical section shows a moderate grade of diffuse cirrhosis and fat infiltration. There are numerous typical fat necroses involving the edges of the lobules. No hæmorrhages are seen. Focal necroses are quite numerous and many polymorphonuclear leucocytes are seen in these areas and in the œdematous stroma. The islands are normal. The duct epithelium shows a metaplasia to a stratified type, and there is some inflammation of these structures whose walls are thick and much dilated. It is possible that there has been an infection of the obstructed ducts, but there could have been no retrojection of bile through the constricted and cancerous duct and papilla.

These 5 cases all show more or less chronic diffuse pancreatitis and focal necroses, suggesting that these are predisposing factors in the development of fat necroses. Icterus is present in 3 cases. The changes in all are rather slight, only one small fat necrosis in the entire pancreas of one case—and can be easily overlooked. Perhaps a more rapid extension of the process would lead to hæmorrhages, and the familiar lesion of hæmorrhagic pancreatitis.

Acute Hæmorrhagic Pancreatitis—7 Cases.

Very brief abstracts of these cases will be given.

(1) Black male, 40 years. (Autopsy, 2820.)

Anatomical diagnosis.—Chronic diffuse nephritis; cardiac hypertrophy; general arterio-sclerosis; bronchopneumonia.

Pancreas is quite pale, but the ducts and parenchyma appear normal. Gall ducts and bladder normal.

Microscopical sections from head, body, and tail show a slight amount of cirrhosis in the head and body, but a more advanced chronic fibrosis in the tail. Duct and islands are quite normal. Section from the tail shows a few minute typical fat necroses and slight extravasion of well preserved red blood cells into the adjacent stroma. *This focus escaped the gross examination. Focal necroses are present in this section, but absent in those from the head and body. Surely this case is closely related to the previous group of fat necroses and probably there is no sharp dividing line. This case again emphasizes the fact that chronic cirrhosis of the pancreas seems to predispose to the focal necroses as well as the fat necroses.*

(2) White female, 13 years. (Autopsy, 2855.)

Anatomical diagnosis.—Bronchopneumonia; acute hæmorrhagic pancreatitis with fat necroses; focal necroses of liver; cystic remains of thyroid; cretinism.

Pancreas presents an unusual appearance. About its distal portion are a few small areas of fat necrosis, one measuring 4. mm. in diameter. The tissue immediately anterior to the body is quite œdematous and of a bloody appearance. The organ measures about 11 cm. in length, and is of normal shape and consistency. The external surface presents numerous lobules, of a whitish yellow color, surrounded by a reddish network. Numerous minute hæmorrhages are present. Other lobules are of a deep brown and purple color, some quite translucent. On cross section the same lobulation is visible as described, but the organ is made up almost entirely of whitish irregular lobules. A few pin-head areas of focal necroses are present. The duct contains a slight amount of gelatinous mate-

rial, but is everywhere clear on dissection with the scissors. It is found to empty beside the bile duct at the ampulla, but is not bile stained. The gall bladder and ducts are normal.

Microscopical sections from various parts of the organ show normal stroma and ducts. All sections show a very diffuse and recent type of hæmorrhagic inflammation and necrosis of the parenchyma and fat cells. The polymorphonuclear leucocytes and red cells are well preserved. Lobules which are not involved by the hæmorrhages show scattered focal necroses of the usual type affecting one or several acini.

(3) White female, 52 years. (Autopsy, 2869.)

Anatomical diagnosis.—Cholelithiasis; carcinoma of hepatic ducts; icterus; dilatation of pancreatic duct; chronic pancreatitis; pancreatic fat necroses; thrombosis of iliac vein.

Pancreas is somewhat enlarged and quite firm. There are numerous hæmorrhages which show through the overlying peritoneum, but which are very small and superficial. Opaque areas of necroses also show through from the pancreatic tissue. On section the pancreas is found to be separated into lobules by a grayish œdematous fibrous tissue. In places the lobules stand quite far apart. There are numerous necrotic patches throughout the gland, the larger being 1 cm. or more in diameter. In these areas the tissue is reduced to a green opaque pulp, which is apparently outlined by a beginning capsule. The necroses are more abundant toward the tail where every section shows a number of them. The pancreas near the head shows fewer of them, and the head itself is practically quite free. The duct is greatly dilated. In the tail it is about 3 mm. in diameter, but toward the junction of the middle and the head, it becomes dilated to 6 to 8 mm. in diameter, contracting again sharply at a sudden curve to a diameter of about 4 mm., which it maintains to its opening at the papilla, which, as stated, lies side by side with that of the bile duct. The ampulla is not so prolonged as to suggest a possible retrojection of bile. There are many branches from this duct, but no special duct of Santorini was found. There is no obvious cause for the dilatation of the duct. Its mucosa looks slightly scarred. It contains a glary opalescent colorless fluid. The very sclerotic splenic artery courses through it.

Microscopical sections show a moderate degree of diffuse cirrhosis. The ducts are dilated and thickened, but show no acute process. The islands appear normal. There are numerous recent and organizing fat necroses in the lobules and at their edges. There is the usual picture of an acute hæmorrhagic inflammation in many areas, but this change is absent in many lobules. Here we may find scattered focal necroses in the acini; some of them are of the hyaline type and quite small as a rule.

(4) Black female, 28 years. (Autopsy, 2775.)

Anatomical diagnosis.—Retroperitoneal and retropancreatic hæmorrhage; disseminated fat necroses; large retroperitoneal hæmatoma; anæmia. Pancreas is of normal size and consistency. Its tail is included in the necrotic hæmorrhagic extravasation. The duct is normal. The parenchyma shows scattered fat necroses. Gall bladder and ducts normal.

Microscopical sections show an advanced type of very diffuse cirrhosis. Large areas of necrosis of fat and parenchyma are seen which are outlined by large wandering cells and fibroblasts—they are evidently of some age. No recent focal necroses are found, but scattered areas in which there has been a disappearance of the acini with replacement by fibroblasts and polyblasts. We may look upon these as areas of focal degeneration or necrosis which are of the same age as the fat necroses and are undergoing organization.

(5) White male, 69 years. (Autopsy, 2812.)

Anatomical diagnosis.—Myelogenous leukæmia; submucous and subserous ecchymoses; necroses in liver; cholelithiasis; acute hæmorrhagic pancreatitis.

Pancreas is considerably enlarged, and greatly softened. It presents a mottled grayish purple appearance due to the fact that there are small recent hæmorrhages between many of the lobules which are swollen, soft and of a grayish pink color. A few minute fat necroses of pin-point size and chalky white color are seen in the gland substance. No fat necroses are seen in the surrounding tissue. The lobulation is hard to make out because of the softening and hæmorrhages, but it seems somewhat irregular. The pancreatic duct is clear and opens freely into a well-formed diverticulum of Vater. A stone could have blocked this opening and caused a retrojection of bile into the pancreatic duct, but there was no evidence of this.

Microscopical sections show considerable post mortem changes which have obscured the details. There is an advanced type of diffuse cirrhosis plus the usual hæmorrhagic change.

(6) Black female, 40 years. (Autopsy, 2879.)

Anatomical diagnosis.—Myocarditis; chronic passive congestion of viscera; pelvic and cardiac thrombi; pulmonary infarcts; liver necroses; hæmorrhages in pancreas.

Pancreas is of about normal size, but very soft and flabby. On section the parenchyma is almost diffluent, but shows here and there scattered areas of purplish hæmorrhage, 2 to 3 mm. in diameter, which merge gradually into the parenchyma. These are most numerous in the body, but present in the head and tail of the organ.

Microscopical sections show a definite hæmorrhagic inflammation of the pancreas with invasion of leucocytes at the edges of these areas. There is a moderate grade of diffuse cirrhosis, but none of the finer changes can be made out because of autodigestion.

(7) White female, 65 years. (Autopsy, 2860.)

Anatomical diagnosis.—Carcinoma of gall bladder (cholelithiasis); invasion of liver, duodenum and common duct; extreme icterus; hæmorrhagic pancreatitis; subserous, submucous and subcutaneous hæmorrhages; bronchopneumonia; liver necroses.

Pancreas is enlarged throughout, but this enlargement is most marked in the caudal portion. In the terminal 5 cm. of the pancreas the organ is found to be greatly enlarged, firm and elastic. It is of triangular cross section, measuring about 4 cm. on a side. The fat in the immediate neighborhood shows a great deal of dark purplish hæmorrhage and some scattered foci of orange yellow opaque chalky appearance. The pancreas itself on section shows numerous opaque chalky dots of varying size and a few areas of blackish green necrosis, measuring 4 to 5 mm. in diameter. Only a few small hæmorrhages are seen in the parenchyma of the pancreas. The hæmorrhages being most conspicuous in the fat in the immediate neighborhood of the pancreas. In one small area about 3 cm. from the tail of the pancreas, the parenchyma and fat near by show a most remarkable change. The tissue is of a mottled appearance, areas of deep purple alternate with yellow opaque areas, or areas of green color, which are usually very dry and chalky. These appear to be older than the areas of yellow necrosis. The body of the pancreas shows hæmorrhages in places, which are usually confined to the subserous peritoneal tissue, but orange yellow necroses are found throughout the parenchyma, varying from pin-head size up to 2 mm. in diameter. As one approaches the head of the gland the change becomes less striking and only occasional foci of orange yellow opacity are found. A few ecchymoses, but no large hæmorrhages are seen in the head of the pancreas. The duct is very carefully dissected out and found to be perhaps slightly dilated. Its intima shows no bile staining. Its wall does not appear to be thickened. The duct opens on the lateral aspect of the bile papilla described above, but their orifices are quite distinct from one another. The pancreatic duct in this location is not thickened and rigid as is the common bile duct. There seems to be some diffuse increase in connective

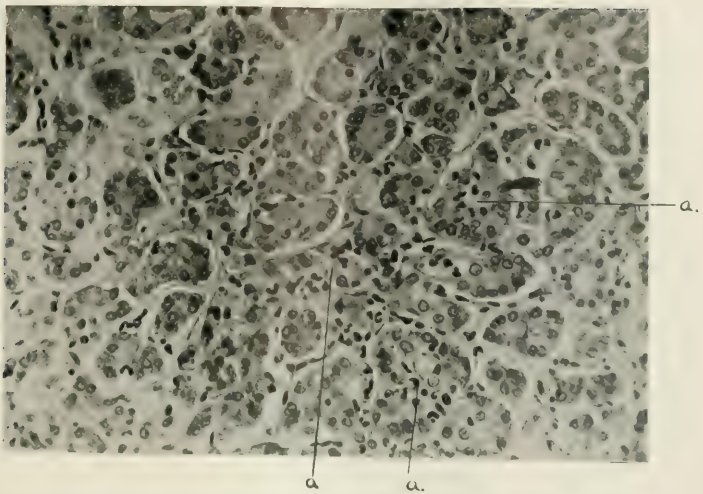

FIG. 1.—Pancreas in case of lobar pneumonia; (*a*) "focal necroses" in acini; cell degeneration and leucocytic infiltration with preservation of the architecture.

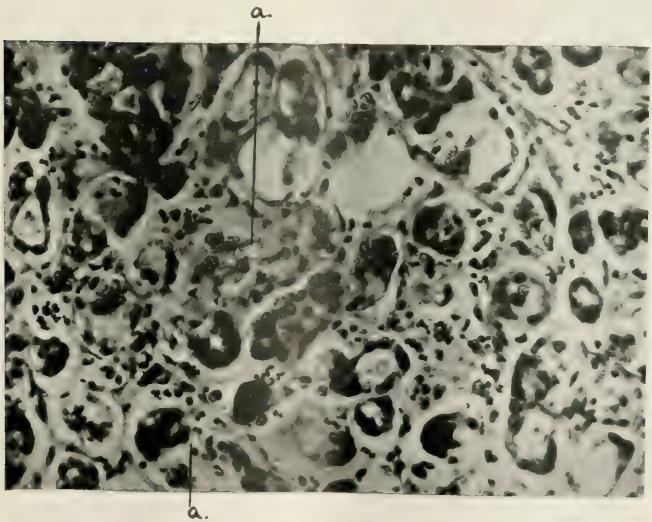

FIG. 2.—Acute diffuse pancreatitis: (*a*) focal necroses in acini. The stroma shows a diffuse infiltration with leucocytes.

tissue between the lobules of the gland, which are definitely glued together.

Microscopical sections show a slight diffuse cirrhosis of the organ. The usual type of fat necrosis and hæmorrhagic infiltration is found, but no focal necroses can be made out in the acini. A few of the smaller ducts show an exudate of leucocytes and a fine granular coagulum in their lumina. They are dilated, and it is possible that there has been an ascending infection from the duodenum, but there could have been no retrojection of bile except by the agency of duodenal contraction.

These 7 cases show several points of interest. The focus of hæmorrhagic necrosis and inflammation may be very small and located in the tail of the organ. Such cases are closely related to those in the previous group of "Fat Necroses." 4 cases show focal necroses in the tissue which is not involved by the hæmorrhage or fat necrosis. 2 cases present so much postmortem change that minute details are obscured. One case shows no focal necroses, but many of the pancreatic ducts give evidence of an acute inflammation. 6 cases show more or less diffuse cirrhosis of the pancreas. 4 cases show liver necroses and 3 icterus. These cases emphasize the relation of chronic pancreatitis and focal necroses to the extensive fat necroses and hæmorrhagic pancreatitis. It is probable that icterus is a predisposing factor. To gain additional evidence on this point a series of 15 cases of icterus was studied. The majority of these cases showed gall stones, or cancer of the ducts. 4 cases presented diffuse cirrhosis and focal necroses; of these cases 2 showed the common type of acute hæmorrhagic pancreatitis. This would indicate the combination of icterus, focal necroses and chronic diffuse pancreatitis as a powerful factor in determining the onset of the hæmorrhagic necrosis.

Chronic Pancreatitis.

An attempt was made to classify the chronic changes in the pancreases in 222 cases. Four classes of cirrhosis were arbitrarily fixed and the pancreatic glands grouped according to the degree of cirrhosis shown by microscopical study. 105 cases showed a perfectly normal stroma.

Class 1. 20 cases showed a very slight grade of diffuse increase in stroma or a few patches of cirrhosis here and there. It is possible that such cases come within the limits of normal gland tissue.

Class 2. 41 cases presented a slight but definite grade of cirrhosis. A single case showed an annular type of change with involvement of the interlobular stroma, but the rest of the cases showed a diffuse interacinar change. A few of these cases showed many dilated acini which often were filled with pink colloid-like casts.

Class 3. 40 cases presented a moderate grade of diffuse cirrhosis involving the interacinar stroma. This change usually caused considerable distortion of the acini with dilatation of their lumina, and the colloid casts were often present. When the acini became dilated their epithelial cells often showed an acid staining finely granular protoplasm and nuclei which were slightly shrunken or normal in appearance. Such cells may make up half the circumference of a dilated acinus while the remaining cells may present the usual granular lilac staining protoplasm and normal nuclei. Because these "acid" cells were often seen in dilated acini filled with a colloid material it was thought that they represented quiescent cells or possibly slightly degenerated ones. With these cells we may compare a different type of pancreatic cell which shows a granular or uniform acid staining protoplasm, and rather dense or normal nuclei. Such cells were seen in about 20 per cent of the tissue examined and they may occur in single acini or large clumps of acini (20-60). These acini did not as a rule show any dilatation and the cells were plump, of normal contour and size. At times an acinus may be found showing these "acid" cells, and the usual pancreatic cell side by side. The significance of these "acid" cells is not clear, but they may be resting cells.

Class 4. 12 cases showed an advanced type of diffuse cirrhosis. 1 case showed an annular type of interlobular cirrhosis but there was a diffuse interacinar change as well. In the majority of these cases the fibrous tissue was dense and poor in nuclei, but in 2 cases it was quite rich in cells and evidently of a more recent formation. The distortion of the acini was great and many peculiar forms were seen. In some cases it seems sure that the acini give off buds which grow into the stroma, and in a few cases mitoses were seen. The small ducts, too, grow into this new formed connective tissue and send sprouts out in many directions, some of which take on the appearance of newly-formed small acini. Many of these cases showed fat infiltration between the shrunken lobules as well as inside the lobules, and cirrhosis of the pancreas seems to predispose to fat infiltration, not depending on the general nutrition. Some cases showed no fat infiltration, even with advanced cirrhosis. Where fat infiltration was found in a comparatively normal gland the general fat deposits were considerable.

Class 5. 3 cases presented an extreme degree of cirrhosis. One was particularly interesting. This case showed a pancreatic calculus situated in the body of the organ. The distal ducts were greatly dilated and the tail of the pancreas was a dense mass of fibrous tissue enclosing a few remnants of acini, ducts, and well preserved islands. The ducts showed great distortion and many buds growing into the stroma. It seems probable that this is a weak effort at regeneration resembling the active efforts of the bile ducts in hepatic cirrhosis. The fat tissue about the tail showed many scars of dense fibrous tissue, and one of these contained much yellow granular blood pigment, suggesting that at some previous time there had been a local area of fat necrosis and hæmorrhage which had undergone complete organization.

The islands of Langerhans were examined with considerable care in all these cases. Very rarely were they the seat of any sclerosis, even when the parenchyma was extremely sclerotic. 2 cases showed hyaline degeneration. Autopsy 2799 was a case of tetanus which showed a slight grade of diffuse cirrhosis of the pancreas. A few of the islands showed a hyaline sclerosis and obliteration, but the majority were normal. Autopsy 2895 was a case of chronic nephritis which showed an advanced diffuse cirrhosis of the pancreas. Many

of the islands in the tail showed hyaline degeneration and sclerosis. Sections from the body showed the same change in the islands, but a smaller percentage were involved. Neither case showed diabetes. 2 cases of diabetes were included in this series. Autopsy 2782 was a case of hemochromatosis with extreme cirrhosis of the liver and pancreas. The islands were quite well preserved, in striking contrast to the acini which showed extreme degeneration, their cells being crowded with yellow pigment which was almost absent in the cells of the islands. Autopsy 2650 was a case of diabetes terminating fatally from a secondary infection. The pancreas showed a moderate grade of diffuse cirrhosis, but the islands were quite normal.

The islands in the following case (Autopsy, 2747) were sufficiently abnormal to deserve mention. The case was that of a strong healthy boy of 6 years who died from a septicæmia developing from a tonsillar abscess. The pancreas presented a normal stroma. The islands were more numerous than normal and of peculiar cylindrical shape, often coiled or twisted. They were made up of double rows of high cylindrical epithelium having pale protoplasm and rather small oval deep staining nuclei situated in the outer third of the protoplasm, near the basement membrane. The limiting membrane was sharply outlined and these cylindrical masses of cells often showed well marked lumina with single rows of cells on each side. In several instances one could trace out a direct connection between the small interlobular ducts and these islands with a gradual transition of epithelium. No islands of the usual type were seen.

4 cases of extreme chronic passive congestion presented some interesting changes in the islands. The capillaries in many islands were dilated to such an extent as to cause almost complete atrophy and disappearance of the cells. Two cases showed hæmorrhage into the capsules of the islands with destruction of the cells, but no rupture of the capsules which were thickened. This was an occasional finding and the majority of the islands were normal.

Conclusions.

1. "Focal necroses" are found in the pancreas in many acute intoxications: pneumonia, septicæmia, peritonitis, typhoid fever. (Fig. 1.)

2. The same necroses are present in acute diffuse pancreatitis (Fig. 2) and in many cases of fat necrosis and hæmorrhagic pancreatitis. It seems probable that these necroses are factors which predispose to pancreatic fat necrosis and hæmorrhage.

3. Chronic diffuse pancreatitis and icterus as well are important predisposing factors.

4. "Focal necroses" and acute diffuse pancreatitis may be the etiological factors in some cases of chronic diffuse pancreatitis.

5. A moderate degree of cirrhosis of the pancreas is a common finding at autopsies.

6. The islands of Langerhans are rarely involved by this cirrhosis.

NOTES ON NEW BOOKS.

Clinical Psychiatry. A Text-Book for Students and Physicians. Abstracted and adapted from the seventh German edition of Kraepelin's "Lehrbuch der Psychiatrie." By A. Ross Diefendorf. New edition, revised and augumented. (*New York: The Macmillan Company, 1907.*)

When Dr. Diefendorf issued his first edition of this book he undoubtedly did great service to the promulgation of the views of Emil Kraepelin and consequently, to the advancement of the clinical method of the study of psychiatry. Before this time (1902) there did not exist any work in English where Kraepelin's views might be studied except in a few isolated instances where a part of his work had been translated, as, for example, Dr. Brownrigg's translation of a part of the section upon dementia præcox. At the time of the first publication of this book the question was asked whether Dr. Diefendorf had been quite fair to Kraepelin in abridging his work and in interpolating matter of his own, but it must be borne in mind that the work of Kraepelin is a large two volume affair and a mere translation would not be as valuable to English readers as an adaptation. Further, the student would not purchase so large a work which would necessarily cost from eight to ten dollars and the time allowed the course of psychiatry in most American medical curricula would not permit of a proper study of such a work. It must be admitted, therefore, that Dr. Diefendorf accomplished the greatest good by his abridgment, and made a text-book which would attract both teacher and student. The objection that by this abridgment the clearness of Kraepelin's views has suffered is not substantiated by a study of the work.

In the present edition considerable new matter has been added from a later addition of Kraepelin and certain parts have been still further abridged as they have been found too full for class room use, for example, the laboratory method of psychological examination has been omitted while the method of general examination has been enlarged by the addition of a number of practical suggestions. There has also been added an abridgment of Kraepelin's chapter on the classification of Mental Diseases, and of the chapter on Psychopathic Personalities which did not appear in Kraepelin's earlier editions. From all standpoints this book is one of the best we have for the student of psychiatry.

In mechanical details the whole is first-class.

W. R. D.

Text-Book of Psychiatry. A Psychological Study of Insanity for Practitioners and Students. By Dr. E. Mendel. Authorized translation, edited and enlarged, by William C. Krauss, M. D. (*Philadelphia: F. A. Davis Company, 1907.*)

This work fulfills many of the demands of popularity in being concise, convenient in size, and reasonable in price, so that there is no reason why it should not meet with success, but while its brevity is of value to the person who wishes to use it as a review, or to enable him to pass an examination, to the student who is first introduced to psychiatry in these pages the brevity may prove a source of confusion unless his teacher is able to go over the book with him page by page and elaborate the knowledge he is acquiring by the examination of considerable clinical material. To the student who has been so fortunate as to acquire a clinical

experience with the insane, this book will be of great value in aiding him to arrange his facts in logical order.

The first 160 pages are devoted to General Psychiatry and are divided into: (a) General Symptomatology, with chapters on Disturbances of Sensation and Sense-perception, Disturbances of Thought, Disturbances of Reproduction (Memory), Disturbances of the Feelings (including Sensory Feelings and Feelings of Judgment), Disturbances in the Condition of the Mind (Emotions), Disturbances of Consciousness, Disturbances of Self-Consciousness, Disturbances of Action, Disturbances of Speech, Writing, and the Expression of the Countenance, Pathological Disturbances in the Condition of the Body, and Anomalies of the Internal Organs; (b) The Etiology of Mental Diseases; (c) Outbreak, Course, Duration, Results of Psychoses; (d) Pathological Anatomy of Mental Diseases; (e) Diagnosis of Mental Diseases; (f) Prognosis of Mental Diseases; (g) General Treatment. A number of the above are also divided into chapters.

The second part on Special Psychiatry occupies 117 pages and is divided into: I. Idiotism, II. Functional Psychoses, III. Psychoses Arising from Central Neuroses, IV. Psychoses of Intoxication, V. Organic Psychoses. As stated in the preface the objection may be made that the above classification "is not wholly free from objection," but will "enable the physician to make a diagnosis in the great majority of cases." This objection is pretty sure to be made by quite a number and especially by those who are accustomed to the classification of Kraepelin, which seems more logical and better defined than that of Mendel.

Quite a number of criticisms may be made of various statements, though in many cases these would be merely expressing a difference of opinion, but the therapeutics as a whole are bad and the free use of the bromides which is advocated, if followed, is bound to produce a number of terminal dements. The use of duboisin and morphia as hypnotics can only be condemned, and the general treatment by hydrotherapy, rest, isolation, occupation, etc., is too briefly touched on.

The work of Dr. Krauss has been well done, and especially in the added matter has he shown good judgment. The supplement containing a form for examination of patients suffering from mental disease is a valuable addition. It is a pity, however, that there are occasional inequalities in the translation which interfere with an easy understanding of the text, the most marked example occurring on page 273. W. R. D.

International Clinics. Vol. II, Series 17. (*Philadelphia and London: J. B. Lippincott Company, 1907.*)

This volume contains 25 articles, four on treatment, medicine, surgery, gynæcology and neurology; three on pathology; and two on pædiatrics; 17 are written by men in the United States, and the remainder by foreigners, among whom may be mentioned Dieulafoy and Letulle, of Paris; Clogg and Lockyer, of England. Cole, Rotch, Flexner, Dock, and Burr are some of the American contributors. Such names as these show how well maintained is the international character of this publication, and its merit. With the constant demands made on the leaders in medicine throughout the world to furnish papers for all sorts of meetings, books, and periodicals, the mark of success of these clinics is in its list of contributors. The first paper in this volume is a timely one on the Vaccine Treatment of Infectious Diseases, by Cole. So much attention has been given to this subject since Wright's original papers, that a careful résumé of the subject, such as Cole here offers, is valuable to all students of medicine. Rous in a similar manner has dealt with The Clinical Examination of the Cerebrospinal Fluid, and in association with this paper should be read Flexner's Experimental Cerebrospinal Meningitis. All the contributions are worth reading, but it is not possible to give the name of the author and title of each. As much praise cannot be given the illustrations, which are often superfluous, and but poor reproductions. One or two good plates are worth a dozen poor ones. R. N.

Nephritis. A Manual of the Disease Commonly Called Nephritis or Bright's Disease, and of Allied Disorders of the Kidneys. By SEELYE W. LITTLE, M. D. (*New York: The Grafton Press, MCMVII.*)

The object of this manual as the author states in his preface is to consider "nephritis as a clinical rather than a pathological phenomenon," and from this point of view Dr. Little has written a useful little book. All readers are not likely to agree that "the disease called nephritis is a step in this evolutionary process towards eliminating individuals with kidneys below a very high standard of efficiency" (p. 32) or that "it is probable that humans have for generations been developing a more and more highly efficient kidney" (p. 33). If this be true of the kidneys, it is equally true of all the other organs of the body, and there is as yet no proof of such evolutionary changes in man. These views of the author do not diminish the good in what he writes, but rather add interest to his work. The Grafton Medical Books are attractively published. They are of a pleasant size and type. R. N.

Notes on Blood Serum Therapy, preventive Inoculation and Toxin, and Serum Diagnosis. For Veterinary Practitioners and Students. By WALTER JEWETT, F. R. C. V. S., D. V. H. (*Chicago: W. T. Keener & Co., 1907.*)

This small book of 200 pages will be of undoubted value to those for whom it is intended. The known general principles of immunity are briefly described and a short statement in regard to the nature of the immunity and the methods for artificially conferring it in each of the best known infectious diseases of animals is given. The discussion is too brief, however, and the statements too dogmatic, considering the tentative nature of much of our knowledge along the lines treated, to make the book of much value to those interested in comparative pathology, or, in fact, to any except those desiring only the most simple and rudimentary knowledge on the subject. The directions, too, for the various diagnostic and other procedures are not given with sufficient detail to make the book of value as a working guide.

The writer is familiar, however, with the latest contributions, and the work of selecting the most important facts have been well done. This small treatise will probably be much used by veterinary students, and is valuable for those desiring to obtain very brief but reliable information concerning immunity in animal diseases.

Foods and their Adulterations. By HARVEY W. WILEY, M. D., Ph.D. (*Philadelphia: P. Blakiston's Son & Co., 1907.*)

Dr. Wiley is so well known to the medical profession as an authority upon the chemistry of foods and the results of his numerous investigations have been so largely appreciated, that this volume, which may be said to express the most positive of his convictions, will find a ready welcome. To those medical men especially interested in questions of public health, the book is thrice welcome, since we have hitherto had in this country no very authoritative expression of opinion upon a number of questions very closely bound up with the national well-being. The book is divided into ten parts, each of which takes up in detail a consideration of a group of allied food products, and it is so conveniently arranged as to afford the reader easy access to the portion dealing with any one particular food. Thus, Part I treats of Meat and Meat Products; Part II of Poultry, Eggs and Game Birds; Part III of Fish Food; Part IV of Milk and Milk Products and Oleomargarine, etc. In these various parts the author has given us an encyclopædic list of practically all the food products known, accurate tables of their chemical composition, data as to their nutritive

value, notices of the various adulterants employed in counterfeiting the genuine article, and finally much technical information as to the chemical substances ordinarily employed in their preservation. In addition to these ten parts, there is an Appendix of over a hundred pages, giving the enactments of the United States Government in regard to the composition of food, the meaning of various trade names and terms, the laws relating to packing and shipping foods, the amount of preservative and coloring matter which may be legally added to food products and a mass of other valuable information. The book is profusely illustrated and these illustrations, with the exception of the colored plates of the various cuts of beef, loaned by Armour & Company, of Chicago, which depart in color very far from the cuts of meat as actually seen in the markets, are fairly well done.

The most interesting and possibly the most valuable portion of the book is Part I, dealing with Meat and Meat Products. Here we find excellent tables giving the composition and the nutritive value of the flesh of different species of animals, of different cuts of the same animal, illustrations of the proper methods of preparing meat for the wholesale and retail market and especially extensive descriptions of the procedures in vogue in canning this product. The subject of preservation is taken up very fully and while we are inclined to agree with Dr. Wiley in the position he takes as to the harmful effects of preservatives upon the animal economy, it is to be regretted that he has not given us more technical information upon a number of points. Many of the original publications of the author upon this phase of the subject have been published in the Reports of the Department of Agriculture and do not find their way into the general literature. For this reason it is important that the reader should be able to obtain in Dr. Wiley's own book, the most convincing results of his many experiments. One would like, for instance, to know the actual amount of various preservatives, such as borax or sulphite of soda, which has been proved to be injurious to man, the amount of such preservatives which has actually been found in meat purchased in the open market, and the percentage of such chemicals which, in Dr. Wiley's opinion, can be added to meat with entire safety to the consumer. The public, unfortunately, is certain to eat meat containing preservatives. How far then will it suffer in so doing? In this section dealing with Meat and also in that treating of Milk, the question of tuberculosis has received inadequate treatment. Because this is undoubtedly the most important problem in the entire range of foods and a lack of agreement among authorities upon some of the minor details is not a good excuse for failure to present the results of countless investigations submitted by scientific men the world over. One looks in vain in Dr. Wiley's book for definite statements as to the amount of tuberculosis in different species of animals, its prevalence in various parts of the country, the harmfulness of the flesh of animals with advanced generalized tuberculosis, the appearance of such tuberculous meat, the harmlessness of meat from animals having localized tuberculosis, and the economic value to the nation of the use of such food under proper precaution by the poorer classes. Again, little is said as to the effect upon man of the consumption of milk from tuberculous cattle, or of the effect of feeding such milk to other species of animals in the propagation of the disease.

In general, however, the information given in the book is adequate and satisfactory, the subject matter is presented with admirable simplicity and the volume is a great credit to the author and may be cordially recommended to the public.

Manual of Clinical Chemistry. By A. E. Austin A. B., M. D., etc. (*Boston: D. C. Heath & Co., 1907.*)

In this small 12mo of 278 pages it is the aim of the author to combine the "practical part" of Medical Chemistry, Physiological Chemistry and the modern methods of analysis, leaving out all that is unnecessary or confusing to the student. The ambition is a laudable one, but we think rather difficult of attainment. In our opinion it is hardly possible to give a student without rather thorough basal training in general chemistry and physics, any material grasp of Clinical Chemistry. And without the knowledge of the reason for various changes and tests, he is likely to be a mere parrot in his work and become a confirmed rule-of thumb text-book diagnostician.

We hardly agree with the author that he has accomplished the task laid down in his preface, and although the book is readable and intelligible to one who is trained, it would hardly fit the student for discerning chemical diagnosis.

Physical Diagnosis. By Howard S. Anders, A. M., M. D., etc. (*New York: D. Appleton & Co., 1907.*)

In this work the author presents a compilation of Physical Diagnosis with no very extensive or valuable personal contributions either in method or interpretation. The reproductions of Butler's plates and the radiograms by Dr. Pfahler are very good, as is the letter press and general appearance of the work.

With many excellent works already available and kept up to date, there seems hardly any pressing need for this.

Hare's Therapeutics. A Text-Book of Practical Therapeutics, with Especial Reference to the Application of Remedial Measures to Disease and their Employment upon a Rational Basis. By Hobart Amory Hare, M. D., B. Sc., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia, etc. New (12th) edition, enlarged and thoroughly revised to accord with the eighth decennial revision of the U. S. Pharmacopœia. In one octavo volume of 939 pages, with 114 engravings and four colored plates. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

Perhaps no other medical text-book which has appeared in the last twenty years has had such a deserved success as Hare's Therapeutics, and it is a pleasure to congratulate both the author and the publisher on this work. It is hard not to feel, however, that the book has lost something in passing through twelve editions, which made the first edition perhaps the best as a student's text-book. This is equally true of Osler's "Practice of Medicine"; in a peculiar charm of its own the first edition surpasses all its successors. Hare's work has grown in size, but has it become really more valuable to the student or practitioner? This growth in size is always a danger to works which are "thoroughly revised" every few years. The author himself is apt to judge ill of what new material needs to be added; he often does not allow sufficient time to elapse to determine the true and permanent value of new discoveries which are daily being made. This mistake in judgment is a natural one, and with the frequent demand for a new edition, it would be almost unavoidable that both author and publisher should feel that the latest information must be set forth, though it may prove before long to be of little value. Had the author been able to give us a revised edition no bigger than the first, it would have been a still better work than the present one, which otherwise deserves all praise. It is one of the few medical text-books which can be thoroughly commended, and which every practitioner will find useful. R. N.

The New Hygiene. Three Lectures on the Prevention of Infectious Diseases. By Elie Metchnikoff. With Preface by Roy Lankester. (*Chicago: W. T. Keener & Co., 1906.*)

This little book contains three lecturers on The Hygiene of the Tissues, The Hygiene of the Alimentary Canal, and Hygienic Measures against Syphilis. They give in a very condensed space the writer's views on the three problems with which his name is most frequently associated, and to our knowledge of which he has made the greatest contributions. As Professor Lankester states in

the introduction, these lectures "should be regarded by the reader as a brief gaze into the mind and mode of work of one of the greatest living men of science." These brief lectures probably reveal more clearly than perhaps any of the writer's other works that which is perhaps at once his greatest strength and his greatest weakness, namely his tendency to construct theories, and to offer hypotheses which are so necessary for the stimulation of further research. Such men are undoubtedly of the greatest value in science. They supply the necessary imagination, which, as President Eliot has pointed out, scientific men frequently lack. Because such men frequently bring forth many hypotheses, and oftentimes persist in their defense against overwhelming evidence, we are too apt to minimize the great value of their work on scientific progress.

As might be expected, the first lecure presents a defense and a laudation of Professor Metchnikoff's favorite offspring, "the phagocytic theory of immunity." The fundamental rôle of the leucocytes in immunity has again been threatened by Wright's discovery that the serum plays an essential and primary rôle in phagocytosis. Metchnikoff, while not denying the occurrence of opsonins, presents evidence tending to minimize their importance and concludes that "we may rejoice that the foundation stone of the hygiene of the tissues, i. e., the thesis that the phagocytes are our avenue of defense against the infective germs, has at last been generally accepted." All will not agree that the evidence entirely justifies his sweeping conclusions, yet most admit that he is partly right, and are willing to forgive the exaggerations. Again, in the second lecture, very great stress is laid on the rôle of intestinal worms in the etiology of certain of the intestinal diseases. He thinks intestinal worms play an important part in the eiology of appendicitis, and even questions whether the entozoa may not serve as portals of entry for the hypothetical parasites of intestinal tumors! In this chapter one is especially struck by the tendency of the writer to lay stress on uncontrolled work and on individual observation. But while the reasoning and the conclusions are undoubtedly somewhat fanciful, and certainly at present not convincing, yet the germ of truth is undoubtedly there, and he accomplishes probably all that he intends, namely, to make the reader think. The last lecture is a discussion of the possibilities of a vaccination or specific prophylaxis against syphilis. At present nothing is definite, but it gives us a vista of the path along which the writer's mind is travelling and of his opinion as to the direction in which the goal probably lies. Any one who is interested in fundamental problems of hygiene cannot help but obtain pleasure and stimulation in reading this volume. Not much is new, but it is well said. On finishing it one has the desire to be up and doing, probably many will have the desire to show that much of it is false, but that proves that the book is of value. It is better to sometimes think wrongly than not to think at all.

Paraffin in Surgery. A Critical and Clinical Study. By WM. H. LUCKETT, M. D., Attending Surgeon, Harlem Hospital, Surgeon to the Mt. Sinai Hospital Dispensary of New York; and FRANK I. HORNE, M. D., formerly Assistant Surgeon, Mt. Sinai Hospital Dispensary. (*New York City: Surgery Publishing Company, 92 William Street.*)

The little book gives in a precise and practical way the technic of paraffin injections, and what is also of importance, discusses the causes of failures and of accidents and the means of avoiding them. The accidents which have followed the injection of paraffin have been few, but they have been serious ones, such as emboli of the lungs, and thromboses of the central artery of the retina, and they will prove a decided objection to the use of paraffin unless a way can be found to avoid them. This way the authors of this book think they have found in using paraffin with a melting point above 110° F.

A large part of the book is given up to the very interesting question of what becomes of the injected paraffin. A number of observers hold that the paraffin is soon penetrated by connective tissue in which new blood vessels are formed and that this newly organized tissue finally takes the place of the paraffin which disappears. Others, who are just as trustworthy, find even after the lapse of several years that the paraffin has not been absorbed. The authors believe that these contrary results are due to chemical differences in the paraffins used, in the varying action of the cells of the body on the paraffin, and on differences in the tissues inspected.

The second part of the book is an account of sixty-four cases of the authors, of some of which a detailed account is given. The photographic reproductions in this part of the book are very poorly done, and are not worthy of it. A full bibliography and index completes the book.

The Technic of Operations upon the Intestines and Stomach. By ALFRED H. GOULD, M. D. (*Philadelphia and London: W. B. Saunders Company, 1906.*)

In this work the author has described all the best known operations upon the intestines and stomach, with various modifications of technic which have suggested themselves to him in his experimental studies on animals and the cadaver. He has added many original illustrations to those drawn from other works on this branch of surgery, and his work will doubtless prove most serviceable to a large body of surgeons, who will find it useful to have these operations so clearly set forth in comparatively small compass. With this book at hand they will be able in a moment to find what otherwise they would have to search for in various works and then not find so lucidly explained. The author is a Boston man and has received much aid from his associates in that city, so that to a certain extent his book presents the views of the surgeons of that city, which adds to its interest. The book should be well received by the profession, for the publishers have done their part as satisfactorily as the author. R. N.

Atlas and Text-Book of Human Anatomy. Volume I. By Professor J. SOBOTTA, of Wurzburg. Edited with additions, by J. PLAYFAIR MCMURRICH, A. M., Ph. D., Professor of Anatomy at the University of Michigan, Ann Arbor. Quarto volume of 258 pages, containing 320 illustrations, mostly all in colors. (*Philadelphia and London: W. B. Saunders Company, 1906.*)

In these two volumes, now out the first devoted to "Bones, Ligaments, Joints, and Muscles"; the second to "The Viscera, including the Heart"; we have the advance publications of what promises to be a complete, I had almost said a perfect atlas for the use of students as well as practicing physicians; as the author states in his preface, "it is not for the finished anatomist, but for those who need a concise, trustworthy, graphic reference," and for these this publication seems ideal. The newer Basel nomenclature is embodied in the work with which we become readily familiar through the necessarily frequent repetitions, and the fact that the old accompanies the new.

The illustrations, and it is the Atlas which is the avowed element in the publication, are most striking, and make the perusal of the books the delightful privilege which this review has proved to be.

The author has been most generous in the number of these exquisite plates, which are good, not only from an artistic point of view, but are graphic and true.

The printers, and binders' art have combined with the author's efforts to supply a publication to which no mere review can do justice, it needs to be seen and read.

Modern Medicine. By WILLIAM OSLER, M. D. Vol. II. (*Philadelphia: Lea Brothers & Co., 1907.*)

The appearance of the second volume of the Osler system will

be welcomed by the profession and gives additional guarantee of the quality of the contributions. The volume covers a very important part of the infectious diseases. Beginning with a most interesting general introduction by Prof. Hektoen, we have a very important discussion of Typhoid Fever by McCrae, which even goes rather extensively into the surgical complications and their treatment. Among other notable sections are Councilman on Smallpox and Chickenpox, Carroll on Yellow Fever, Shiga on Bacillary Dysentery, and Acute Rheumatism by Poynton.

There is much to praise and little to criticize in the collection. The quality of the colored plates is, as in the first volume, inferior, and not up to the standard of the letter press, nor to the credit of the publishers. The photographs and black and white work are good.

Poynton, in his article naturally lays rather more stress on the "Diplococcus rheumaticus" than many competent and careful investigators are willing to concede. Ruhräh gives an excellent discussion of Measles but passes over the mooted "Fourth Disease" rather too briefly. The monograph of Musser and Norris on Lobar Pneumonia is exhaustive and contains all of importance that is in the literature. It is perhaps a little too rich in statistics.

Careful perusal of the introductory chapter and the special section on the pathology of the different specific infections will do much to explain the rational therapeutics most of the writers have suggested. It ought to give the practitioner the courage of conviction in withholding many obsolete and more new and pseudoscientific methods of pouring in drugs to "cure" a self-limited disease, while at the same time encouraging him to observe carefully and meet rationally the emergencies as they arise.

American Practice of Surgery. A Complete System of the Science and Art of Surgery. By Representative Surgeons of the United States and Canada. Editors JOSEPH D. BRYANT, M. D., LL. D.; and ALBERT H. BUCK, M. D. Vol. III. (*New York: William Wood & Co., 1907.*)

This third volume contains Parts XI, XII, and XIII, dealing with "poisoned wounds, including the bites and stings of animals and insects," "injuries and surgical diseases of bone," and "diseases and injuries of joints." The parts are divided into chapters, each by a different author, so that there are eleven contributors to this volume, among whom are such well-known men as Major and Surgeon Charles F. Mason, U. S. A.; J. C. Oliver, C. F. Painter, Roswell Park, Duncan Coe, etc. The work is abundantly and excellently illustrated, but we fear that due to the clumsiness and weight of the volume, the articles will not receive the attention which is their due. It is a pity that this system which is so valuable as setting forth the views of many of the leading surgeons in America should not have been published in a more handy form. In such systems it is difficult to compare the relative merits of different chapters, for so much depends on the instructions given by the editors to the contributors. One writer may be allowed many pages for his article, and another far fewer, though the two subjects may seem of equal importance to many readers. The amount of space allowed to different subjects in the first three volumes seems to have been well adjusted, and there is an "up-to-dateness" in the papers which is satisfactory. Each volume is supplied with its own index. This system, with all the drawbacks common to all systems, is to be recommended to the profession. R. N.

Principles and Application of Local Treatment in Diseases of the Skin. By L. DUNCAN BULKLEY, A. M., M. D., etc. Small 8vo., 142 pages. (*New York: Rebman Company.*)

This book is the outcome of the requests on the part of his students, for Dr. Bulkley's lectures on local treatment of skin diseases, and forms a companion to his lectures "On the Relation of Diseases of the Skin to Internal Disorders."

The treatment of only seventeen diseases is given. These are characteristic, however, and serve to illustrate the principles underlying local treatment.

The work is based entirely on the author's personal experience, and naturally, some of his ideas differ from other dermatologists'. However, many excellent suggestions are offered which will doubtless prove of much value.

It is interesting to note that, though polypharmacy is decried, no less than forty drugs are mentioned in the treatment of eczema. While this, of course, is a large number, it bears eloquent testimony to the obstinacy of some cases of this disease.

INDEX TO VOLUMES 1-16 OF BULLETIN.

A subject and author index of the first sixteen volumes of the Johns Hopkins Hospital Bulletin is now ready. As the edition will be limited, it is desirable that orders be sent in as promptly as possible.

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ON TELANGIECTASIS CIRCUMSCRIPTA UNIVERSALIS.

By William Osler, M. D.

For many years I have been interested in the nævi and small telangiectic spots which one sees so frequently in the routine examination of patients. Their increase as age advances, their peculiar distribution, their temporary character in young persons, the association with cirrhosis of the liver, the possible association with internal carcinoma, the occasional eruptive-like outbreak in jaundice, the remarkable hereditary form associated with epistaxis (of which I have reported three cases)[1] the presence of the spider-nævi in scleroderma, and their occurrence in the scar of X-ray burns—these are points upon which I have dwelt over and over again in the routine work of the wards. On January 21, 1906, while I was taking one of Dr. Barker's ward classes, I found a patient whose case is here described, and I saw immediately that it was a form of generalized telangiectasis which I had never met with before. The case belongs to an excessively rare form of the disease of which only some fifteen or twenty cases are on record, and Dr. Barker has very kindly allowed me to report it. The history may be given in full:

W. J. H., age 39.—Patient complains of pain in the right side of abdomen.

F. H.—Family history is negative. The parents are living and well. He has no brothers nor sisters. His parents deny emphatically any joint or skin trouble in the family, but the mother had urticaria when young.

P. H.—Patient has not had any infectious disease. He has not had tonsillitis. He had attacks of "grippe" for several consecutive winters. The first, during an epidemic in Paris in 1889, was severe. In 1893-94 he had "pleurisy" though from his description one would suspect it to be lumbago. The pain was in the lumbar region, chiefly in the right side, very severe, relieved by hot packs and turpentine, in many ways resembling his present pain except that the former attack has been entirely in the back. He has believed his back to be weak and has taken gymnastic exercises. He has always been of neurotic temperament, and after 3½ years of hard work with much privation as an artist in Paris he broke down in 1893 with "nervous prostration," and for six years could work only intermittently. He thinks he has never entirely recovered.

Head.—He has had attacks of giddiness about once a week for past three years. He has considerable astigmatism which causes severe headaches relieved by glasses. Has never had any flashes of light; has never fallen; never has vertigo; no ear trouble.

Respiratory system.—No chronic cough, bronchitis, or haemoptysis.

Cardio-vascular.—During the past three months he has been rather short of breath after meals and on running up stairs. No pain around the heart.

Renal.—Not any oedema of ankles or of face. No blood in urine before present illness. The urine has been examined several times in the past few years and always found normal. No increase in frequency.

Gastro-intestinal.—No symptoms on the part of these organs; bowels always regular.

Habits.—Until six years ago he was an excessive smoker; since then moderate. Formerly a moderate drinker; now abstemious. Denies all venereal trouble.

Skin.—The skin condition has evidently not attracted much attention. The patient states he had noticed the purplish mottling only for the past ten years. His mother is sure that his

[1] Johns Hopkins Hospital Bulletin, 1901, Vol. XII, 333.

skin was normal when a baby and during youth and she has noticed the present condition only during the past two years. The patient says the mottling has become more intense during this time. At no time has it entirely disappeared, although more intensely colored during cold weather than in summer. During the summer of 1889 he had an attack of hives, and he gives an indefinite history of several attacks since. In November, 1905, he began to have epistaxis which has recently recurred without apparent cause and lasting about five minutes. During his attack of "nervous prostration" he was troubled with hæmorrhoids and was operated on. He has never noticed any tendency to prolonged bleeding from slight cuts. Has never had hæmoptysis. He denies absolutely any attacks of joint pains, colic, vomiting, or diarrhœa.

During the past month the patient's feet have bothered him by intense itching, so severe as to cause him to rise at night and apply a lotion. During the past two weeks patient has undergone a great deal of mental and physical exhaustion in connection with an art exhibition.

P. I. —Came on suddenly at six o'clock in the morning of January 20 (yesterday), with the passage of about a pint of bloody urine (dark red), followed by pains in the right abdomen "just below the last rib on the right side." Gradually the pain became extreme, and in ten minutes was at its height, causing the patient to double up and roll about in agony. The pain remained localized and did not radiate to the thighs or shoulder, nor was it paroxysmal. The pain lasted about twenty minutes and then gradually ceased, the patient breaking into a free perspiration. In half an hour after the onset of the pain he felt all right again, arose from bed and went about his days work (mounting and selling pictures). Last night he retired at 11.30. During the day patient passed his water three times and while it appeared dark, he did not notice that it contained blood. Last night the patient slept fairly well and did not get up to urinate. About six o'clock this morning (January 21), patient had a peculiar sensation in right abdomen, and a "presentiment of another attack." He arose from bed and passed another pint of brick-red urine, during which passage there was no pain, but immediately afterward pain came on gradually and in five minutes was extreme. A doctor was summoned who diagnosed the case appendicitis. The pain was agonizing and this time lasted five hours (until morphine was given sufficient to relieve it), and was accompanied by fever. The patient does not remember that he was short of breath during the attacks. In the first attack he had considerable nausea but was unable to vomit. In the second attack he vomited freely, especially after taking morphia. He has had no diarrhœa with the attacks. His appetite is good and he says it always has been.

Since the onset of his trouble the patient has noticed a prickly sensation in the end of his penis on urination.

Patient's mother says that the urine passed in the first attack contained blood definitely, but she is quite sure there was no blood in the urine passed before the attack on the second morning.

Fairly well nourished man. Face rather flushed: keeps eyes closed: pupils rather wide. *Pulse* 68, with occasional slight irregularity. Vessels well felt but not sclerotic.

Thorax.—Is symmetrical, except that right side is slightly fuller than left, and sternum deviates slightly to left. There is a well-marked lateral curve to right in mid-dorsal region. Movements of chest are equal. Lungs clear in front.

Heart.—Apex impulse visible and palpable in fifth interspace about in mammillary line, 9.3 cm. from median line and dulness extends 3.7 cm. to right. Impulse is of moderate intensity. First sound at apex slightly prolonged, suggesting a systolic murmur. Second sound clear. Sounds are clear elsewhere. Second left or pulmonic, a little louder than second right. During examination a number of patches of urticaria have appeared. There is fairly well-marked dermatographia and where he has been blue-penciled there is urticaria, which is appearing also as wheals bordered by a wide blush over places marked for dermatographia. *Abdomen* is natural. *Liver* is not palpable or enlarged. *Spleen* is readily palpable, falling, with patient on right side, 3-4 cm. below costal margin. The tenderness previously present has now disappeared.

R. B. C.....5,320,000
W. B. C.....11,900
Hb. .....106 (corrected).
Coagulation time = 4 mins. (slide method).

Fresh blood cells.—Appear of good color and uniform in size and shape. Not much tendency to rouleaux formation nor crenation. Leucocytes rather numerous but no marked leucocytosis.

On January 24 I made the following note: The skin presents a very remarkable appearance. On the face there are a few spots like acne rosacea. The skin of the neck is clear. Over the trunk and the extremities are numerous dark red spots looking exactly like a fresh purpura. Their distribution is very well shown in the accompanying photographs. They are very thickly set over the chest and back and on the flexor surfaces of the forearms and inner aspects of the arms (Figs. 2 and 3). The spots vary in size from two to six millimeters in diameter, and often coalesce to form large blotches. While of a dark purplish tint, as a rule, they can be changed by rubbing to a vivid red. Everywhere on palpation the spots disappear completely, leaving a slight brownish stain. They are not raised and the color is uniform. There are no individual blood vessels seen. It is evidently a capillary dilatation. It is remarkable the difference in appearance after friction of the spots on the arm. They become of a bright red color, return instantly after pressure, while the other spots are of a dark livid hue and the blood returns very slowly. The condition of the hands and feet is very remarkable. As seen in Fig. 1, the fingers are cyanotic and look like the picture of Reynaud's disease. The soles and margins of the feet and the toes have the same deep purple color. Factitious urticaria is readily produced, as is well shown in Fig. 4. The patient remained in hospital until March 9. He was on a modified Weir Mitchell treatment and did remarkably well. Dr. Bordley reported that he had a slight choroiditis in the right eye. During his stay in the hospital the patient had several severe attacks of abdominal pain, which was relieved by acupuncture. I saw the patient again an January 2, 1907. The skin was in practically the same condition. Though still somewhat nervous, he had kept pretty well and was able to attend to his work. The best account I have found of this condition is in *La Practique Dermatologique*, T. IV, by Brocq, under the title of Primitive Generalized Telangiectasis. Very few of the reported cases have had anything like the same extensive distribution as in the one here described. In one reported by Vidal[2] he calls it *Telangiectasie accidentale symétrique et généralisée*—a female, aged 31, nervous and hysterical; at the age of fourteen noticed the red spots appearing under aspects of the forearms. They extended gradually

[2] Bull. d. la Soc. Méd. des Hôpitaux, 1880-81, page 186.

FIG. 1.

FIG. 3.

FIG. 2.

FIG. 4.

and appeared symmetrically on the arms, chest, neck, fingers, the backs of the hands, and the lumbar and dorsal regions. Before they came out she was very much troubled with a chronic urticaria, and she had a very marked hyperæsthesia of the skin. Levi[3] has reported two cases, the second one, a woman, aged 33, had only 35 spots in all, which had appeared in different parts of the body between 1897 and 1900. In his first case, a woman aged 70, the spots were much more extensive, and with a distribution very much as shown in the photographs here given, but there was not the extreme involvement of the feet and hands.[4]

One or two points about this case require comment. From the statement of the mother there can be little question that this is an acquired, not congenital form. Everywhere it is the capillaries, not the small venules that are involved. The appearance of the back and of the arms is not unlike that seen in the most extreme grade of vasomotor mottling. The patient, Juliet D., medical number, 16254, who was in the ward G in October, 1903, had an appearance of the back and feet very similar to this patient. She was also extremely neurotic, but under treatment the mottling entirely disappeared. This is a permanent dilatation of the capillaries of localized areas. The condition of the hands and feet suggests the local asphyxia of Reynaud's disease. The skin of the soles of the feet and the toes was quite purple. The color could be changed to a vivid red by friction. In the interval of a year, which elapsed after I first saw him, no change had occurred, so that it is evidently a state of permanent ectasia of the blood vessels of the skin. Dermatographia, common enough in conditions of vasomotor instability, is seen in a marked degree in many cases of neurasthenia. Two other symptoms are of special interest in the case. The recurring attacks of colic, for which no cause could be found, may have been associated with a gastro-intestinal urticaria, that is a localized area of infiltration of the gastro-intestinal wall, such as has been shown to be responsible for the colic in the so-called Hennoch's purpura. The hæmaturia may be a form of so-called renal epistaxis, such as is met with sometimes in Reynaud's disease. Bleeding is a common event in the remarkable generalized telangiectasis of the hereditary form, and some of the cases have been described as hæmophilia. Since the report of the cases in the *Bulletin*, already referred to, I have found another family. The bleeding is usually from the nose, but it may be from the lips or mouth, only rarely from the spots on the skin.

[3] Gaz. Hebdom., 1901, p. 13.
[4] Presse Médicale, 1896.

POSITION OF THE HEART IN PERICARDITIS WITH EFFUSION.

By W. J. Calvert, M. D.,

University of Missouri, Columbia, Missouri.

The position of the heart in pericardial effusions is of practical importance in tapping the sac. Consequently observers have, from time to time, attempted to determine its position and most naturally have arrived at various conclusions. Skoda (1) and his followers think the heart is displaced downward and backward. Schaposchnikoff (2) and others say the heart is pushed upward, anteriorly and may be in contact with the anterior thoracic wall. While a third group (3) contend that the heart remains in its normal position.

This difference in opinion indicates that the heart in pericarditis with effusion occupies various positions, which must be determined by physical factors or laws. These factors change or vary with the changing conditions within the pericardium. If these physical factors or laws can be determined and if clinical observations can be interpreted in terms of these laws, the position of the heart in a given case of pericarditis ought to be fairly accurately determined.

The aim then of this article is to determine, as far as possible, the physical factors which govern the position of the heart in pericarditis.

Material.—The material for this article was obtained through the kindness of Dr. C. M. Jackson, to whom I wish to express my thanks. The material consists of the cadavers of two individuals who, at the time of death, had pericardial effusions. The cadavers were hardened by an intra-arterial injection of formalin and sectioned transversely. From these sections drawings and measurements were taken by means of which the organs have been projected. This material is designated as Cases I and II. The two cases were treated in exactly the same manner, consequently any changes in the cadavers due to manipulation should be the same in each.

Three pictures showing the position of the heart in pericarditis with effusion are reproduced from the Anatome Topographica, by Nicolao Pirogoff, published from 1852 to 1858. I wish to express my thanks to the library of the Surgeon-General's office for the use of this atlas.

Case I.—The cadaver is that of a fairly well built male negro, aged thirty. A left sided pleurisy with a very small effusion, adherent right pleurisy and pericarditis with effusion were observed.

The position of the pericardium is shown in Figs. 1, 2 and 3 It extends from the second to the seventh rib in the left mammary line, and the seventh rib in the right sternal line; the lungs have been displaced outward, and the diaphragm downward.

All of the chambers of the heart are collapsed (Figs. 1 and 3). The heart is against the posterior wall of the pericardium, separated by fluid from the anterior wall. In Fig. 2 (anterior projection) the upper border of the heart is at the top of the third rib; apex, six centimeters from the mid-sternal line; the right

border, three and three-fourths centimeters to right of mid-sternal line; and the lower border on a level with the seventh rib. The apex is displaced backward and slightly to the right (Fig. 3). The downward displacement of the diaphragm has not been followed by the heart. There are no adhesions between the heart and pericardium.

The venae cavae are collapsed as shown in Fig. 1, *f*, and *i*. The vessels are collapsed from their entrance into the pericardium to the heart. Their lumen may be represented by a Y-line. Outside the pericardium the veins are congested.

The lumen of the aorta is obliterated, flattened in the anterior-posterior diameter.

The pulmonary arteries and veins are congested outside the pericardial sac.

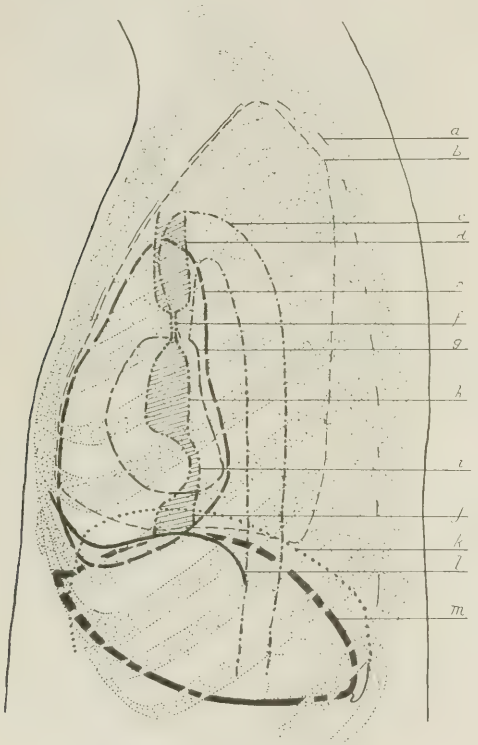

FIG. 1.

CASE II.—Cadaver is that of a male negro, aged twenty-nine, well formed and fairly well nourished. Examination revealed tuberculous consolidation, with multiple small cavity formations in the left lung, and pericarditis with effusion.

The pericardium extends from the middle of the first interspace (mid-sternal line) sixteen and one-half centimeters downward, almost to end of the sternum; eight and one-half centimeters to left and six and one-half centimeters to right of mid-sternal line. Its relationship to the anterior thoracic wall and the lungs is well shown in Figs. 4, 5, 6, and 7. The lower wall of the pericardium is pushed downward with the diaphragm (Fig. 4).

All of the chambers of the heart are distended with blood (Fig. 6). The position of the heart in an anterior-posterior diameter and its relationship to the anterior thoracic wall and lungs are sufficiently well shown in Figs. 5, 6 and 7, to dispense with further description. The projection of the heart (Fig. 4) extends from the upper border of the third rib to the articulation of the seventh costal cartilage with the sternum, six and three-fourths centimeters to the left and five centimeters to the right of the mid-sternal line. The heart is in a relatively normal position. The lower wall of the pericardium has been displaced downward leaving the heart absolutely free to support itself in the pericardium (Fig. 4). There are no adhesions between the heart and pericardium.

The venae cavae are distended throughout and continuous with the distended right auricle (Figs. 4, 5 and 7).

The aorta is distended (Figs. 4 and 5).

The pulmonary arteries and veins are distended (Fig. 5).

COMPARISON OF THE TWO CASES.

FACTORS IN COMMON.

1. The pericardial sac is distended relatively the same in the two cases; neither of them are large effusions.
2. Pulmonary congestion in each.
3. Systemic venous congestion in each.
4. In each the heart is free in the pericardium, consequently uninfluenced by adhesions.
5. In each the projection of the heart on the anterior thoracic wall shows a relatively normal position.
6. In each the heart was completely surrounded by fluid, consequently the buoyant force was relatively equal in the two cases.
7. In each case the heart swings in the sac absolutely independent of the lower wall of the pericardium and diaphragm.
8. Gravity must have been equal in the two cases.
9. A dorsal position of the two patients at the time of death may be assumed. When the cadavers were injected and hardened, both were in the dorsal position.

DIFFERENCE IN FACTORS.

Case I. Heart chamber collapsed.
Case II. Heart chamber distended.
Case I. Heart displaced backward not in contact with anterior thoracic wall.
Case II. Heart immediately behind the anterior thoracic wall, practically in its normal position.
Case I. Venæ cavæ within pericardium collapsed.
Case II. Venæ cavæ within pericardium distended.
Case I. Left auricle collapsed.
Case II. Left auricle distended.

SUMMARY.

Case I. Heart and vessels collapsed. Heart against posterior wall of pericardium, in posterior position.

Case II. Heart and vessels distended, in relatively normal position.

A casual consideration of the two cases shows that:

1. The heart may or may not be in its normal position.
2. That it is not displaced upward to the anterior.

3. That it does not sink downward when the support of the diaphragm is withdrawn.

4. When not in the normal position the heart is displaced backward against the posterior pericardial wall.

5. The distension of the heart's chambers vary under varying conditions.

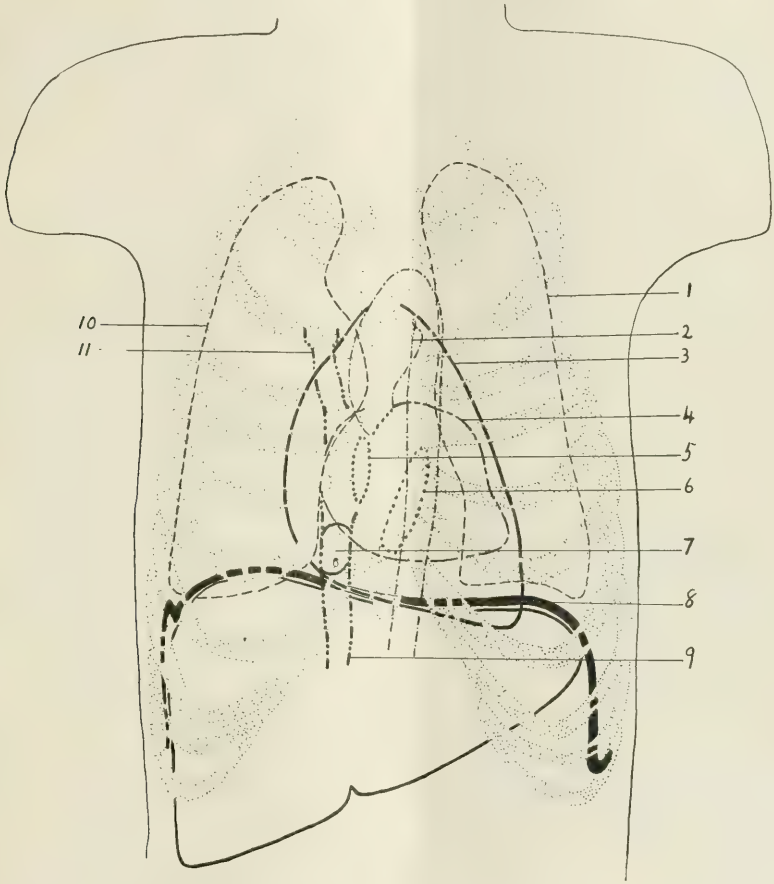

Fig. 2.

The circulatory changes herein considered have been studied in the light of physiological and clinical data. In this consideration the heart is supposed to be free from valvular lesions. The order of description is: left auricle, right ventricle, right auricle. The left ventricle is considered in the paragraphs on compensation, amount of blood delivered to the ventricles, pulse rate, etc.

Left auricle.—When the pericardial pressure first affects the auricle, the auricle must be compressed to a point where the intra-auricular pressure equals the pericardial, or the auricular pressure is increased and must cause pulmonary congestion. While compensation is maintained a normal quantity of blood is delivered to the auricle which must remain relatively normal in size. The auricular pressure must increase as the pericardial increases; and at no time can it be less, else the auricle must collapse, when death would follow. As compensation fails and less blood is delivered to the right heart, the auricle diminishes in size, until practically no blood reaches it, when it is collapsed as in case I.

The pulmonic congestion must vary with the pressure in the left auricle, consequently must continue throughout the course of the disease.[4]

Right ventricle.—The right ventricle must pump its blood into a high pressure pulmonic circulation. To accomplish this increased work a certain amount of hypertrophy and perhaps some dilatation are necessary.

Right auricle.—The right auricle and venæ cavæ within

the pericardium are subjected to the pericardial pressure and must be compressed, this obstructs the flow of blood from the superior and inferior cava, causing a congestion and rise of blood-pressure within the systemic veins. This increased venous pressure must compensate the effect of the pericardial pressure on the auricle and venæ cavæ within the pericardium. So long as this compensation continues a relatively normal quantity of blood flows to the right auricle, thence to the right ventricle. But when this compensatory congestion begins to fail the lumen of the vena cava within the pericardium becomes progressively smaller, consequently less and less blood flows to the right auricle, thence to the right ventricle. The quantity of blood entering the right auricle must determine the quantity of blood in the heart. The pressure within the right auricle must be like that in the left, slightly greater than that in the pericardium, consequently the pressure in the systemic veins must be above that in the pericardium, and must offer an opportunity to measure the pericardial pressure. The right auricle, like the left, is gradually compressed by the effusion, until collapsed, all the while maintaining a high auricular pressure.

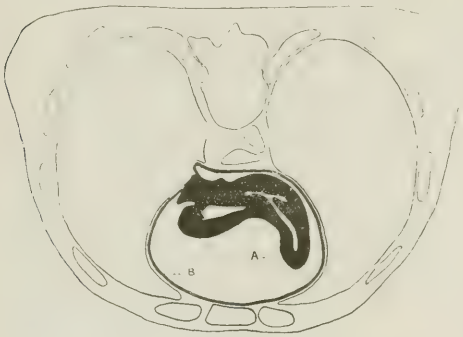

Fig. 3.

Compensation.—To complete the cardiac circulation the blood must enter the pericardium twice, consequently the pericardial pressure must be compensated twice:

1. The left auricle is compensated by the right ventricle.

2. The right auricle, by the increased pressure in the systemic veins due to congestion.

As the two mechanisms for compensation are independent each may remain competent while the other fails. If the right ventricle fails, while the venous compensation is competent, the right auricle would continue to pump blood into the right ventricle, which would dilate, but would force little or no blood to the left heart, which must collapse. Traube[3] describes a case illustrating this point. He says: "The heart is very small, and peculiar in that the diameter of the base is greater than the longitudinal diameter. The contents are fluid and large in quantity on the right side."

If the venous compensation fails little or no blood enters the right heart, a like amount, the left. Consequently the heart must gradually collapse, because there is not enough blood to distend it. This is shown in case I.

Blood delivered to ventricles.—The amount of blood delivered to the ventricles must depend on the degree of compensation. In the early stages of the disease the auricles are perfectly compensated with perhaps a slight margin of reserve force. During this stage a normal amount of blood should be delivered to the ventricles. (On account of the increased auricular pressure a slightly increased amount of blood may flow into the ventricles.) As compensation fails a diminished amount of blood is delivered to the right auricle, consequently to the ventricles.

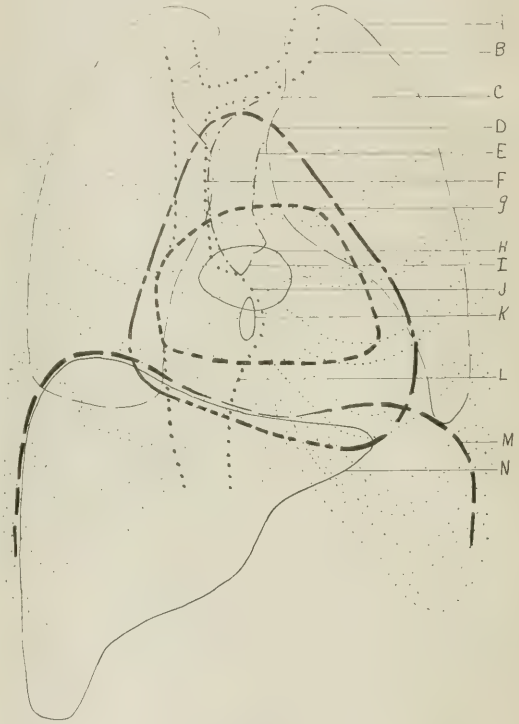

Fig. 4.

Pulse rate.—The pulse rate is usually increased throughout the course of the disease and is due to different causes in the several stages of the disease.

1. In the beginning the ordinary febrile pulse must be present.

2. The distension of the large veins is a sufficient mechanical stimulus to increase the heart's action.

3. As the amount of blood entering the heart diminishes a low arterial tension develops. This the heart attempts to compensate by increased activity.

4. If the venous pressure becomes very high a reflex diminution in pulse rate may follow.

5. If the vagus is involved a slow pulse rate may develop.

Blood-pressure.—When the pericardial pressure is first developed, the high pressure in the auricles may for a time deliver to the ventricles more than the normal amount of blood which, with the increased rate of the heart, may give an increased arterial tension. If this is true, it is only temporary. When compensation has developed, a relatively normal blood-pressure should be maintained. Hensen[6] reports a normal blood-pressure in two cases with large effusions. As compensation fails the arterial pressure falls; or the arterial tension falls as the pericardial pressure rises. This decrease in arterial tension was first experimentally demonstrated by François Frank.[1]

Coronary circulation.—The coronary vessels are subjected to the direct pericardial pressure, and the flow in the veins is obstructed by the increased auricular pressure. These factors must seriously interfere with the coronary circulation, more especially in the later stages of the disease, when the arterial tension becomes much diminished. There is no compensation for this impediment to the coronary circulation. The resulting anæmia may in large measure account for the myocardial changes noted.

Work of the ventricles.—While compensation is maintained the pulmonic blood-pressure is higher than normal, the systemic blood-pressure normal. Consequently the right ventricle has an increased amount of work to do, the left a normal amount. As the disease progresses and compensation fails the pulmonic blood-pressure is increased, the systemic decreased. The right ventricle has an increasing, the left a decreasing resistance to overcome.

Position of the heart.—In the cited cases the heart is shown in positions ranging from relatively normal to that shown in Case I, or completely collapsed and against the posterior wall of the pericardium. In each of the two cases described the heart is supported by the large vessels, in one it is collapsed, in the other, distended; consequently the degree of distension of the heart must determine its position in the pericardial sac; or the position of the heart depends on the cardiac hydraulic pressure acting against the attachments of the heart, and the amount of blood within the heart and that portion of the large vessels within the pericardium. The distension of the heart depends on the amount of blood delivered to the right auricle; this amount of blood depends on the compensatory venous congestion; and the latter depends on the relationship between the intravenous and pericardial pressures. So long as compensation is maintained the degree of pericardial pressure is not important; but as compensation fails the quantity of blood delivered to the right auricle varies inversely as the pericardial pressure.

In the standing position the greater portion of the weight of the heart and its blood is supported by the aortic and pulmonic arteries. The distended auricles fastened behind to the pulmonary veins and on the right above and below to the venæ cavæ, act as a brace or prop to keep the heart from falling backward on account of gravity. In the dorsal position the weight of the heart is transmitted through the distended auricles to the large veins, thence to the mediastinal tissues and the vertebral column. Here the aorta and pulmonary artery, attached anteriorly to the base, act in a measure as a prop to prevent side to side movement of the heart.

During the stage of compensation the quantity of blood in the heart remains fairly constant, consequently the position of the heart must remain as constant. (If the heart was in a normal position at time of onset of effusion it must remain in relatively a normal position while compensation is maintained.) But as compensation fails the quantity of blood delivered to the heart must gradually diminish, allowing both the auricles and ventricles to gradually diminish in size. This process continues until the heart is completely collapsed. The auricular brace above described becomes shorter, which allows the heart to swing backwards on the aorta and pulmonic artery as a hinge. The apex is displaced backward. The shortening in the long diameter of the heart probably compensates the downward displacement of the apex, due to its partial revolution about the aorta. Thus the apex is displaced backward and slightly to the right, but not downward or to the left.

During the course of the disease the heart occupies positions varying from normal to that shown in Case I, which is the greatest possible displacement of a normal heart by pericardial effusion.

To determine the pericardial pressure, or the state or stage of the compensatory congestion, is the surest method of obtaining reliable information concerning the position of the heart. This pressure is produced by:

1. The strength of the pericardial walls. Naturally, this factor must vary in each case and must determine the size of the effusion. If the sac can resist a pressure greater than that in the systemic veins, the sac will not dilate and the veins will be closed. If the sac is weak, it will easily dilate and allow the accumulation of a large effusion. In the former condition a high pressure may be developed early; in the latter, late or never.

2. The force under which the fluid enters the sac. Here the question of transudates, exudates, and osmosis have to be considered. They lead to no definite conclusions. That considerable pressure can be developed in the pericardium is certain.

The degree of pericardial pressure may be approximated by:

1. Shape of pericardial dulness. When pressure is high dulness must extend high, first or second interspace, and be triangular. When pressure is low the area of dulness is more quadrangular (Romberg, p. 370), and the movability of the dulness with change of position should be greater. The amount of fluid is of secondary importance.

2. The degree of venous congestion must be an index to the pericardial pressure.

3. Arterial tension should be low when pericardial pressure is high and should decrease as pericardial pressure increases.

Pulsus paradoxus indicates a pericardial pressure relatively equal to the maximum venous pressure.

4. The pulmonic symptoms should be more pronounced under a high than under a low pericardial pressure.

Support of the heart.—Regarding the normal support of the heart, the general opinion is that it is supported by the large vessels, pericardium, lungs, and the central tendon of the diaphragm. The two cases at hand show beyond a doubt that the heart is supported without the aid of the pericardium, lungs, or the central tendon of the diaphragm. Here it is natural to ask can the heart be supported under normal conditions without the aid of these structures?

It has been shown that while compensation continues the heart remains in its normal position and receives its normal amount of blood. During this period the pericardial pressure may vary through quite a wide range without changing the conditions of the heart. It is natural to suppose that compensation is an attempt of nature to maintain as long as possible and as near as possible the normal results of physiological activity. Consequently the increased cardiac and venous pressures are increased after and in proportion to the rise in pericardial pressure and counterbalance the pericardial pressure without taking any part in the support of the heart, in either of the two cases under consideration; and that the normal pressures and quantity of blood remain in the heart in addition to or above the pressure caused by the rise of pressure in the pericardium.

This leaves the normal cardiac pressure and amount of blood in the heart to support the heart in the two cases under consideration and permits the subtraction of the pericardial pressure and a like amount from the cardiac pressure without materially changing the position of the heart. This reproduces the normal condition (save the presence of the fluid) with the heart supporting itself without the aid of the pericardium, lungs, or diaphragm. Now suppose the pericardial fluid is withdrawn without changing the pressures, the walls of the pericardium come in contact. It is reasonable to suppose the heart continues to support itself without the aid of the neighboring structures.

Clinically it is well known that the heart moves a number of centimeters to the right or left as the case may be, consequently the support of the lung and pericardium cannot be very substantial.

If this be true the heart is independent, save in a most general way, of the pericardium, lungs, and diaphragm, and swings free in the pericardium to be influenced by a most delicate mechanism, namely the flow of blood to the heart, the cardiac pressure, and all in the thoracic cavity in which a slightly positive to a slightly negative pressure is maintained.

SUMMARY.

1. The position of the heart in pericarditis depends on the size of the heart.

2. The size of the heart depends on the degree of distension, or on the amount of blood within the heart.

3. The amount of blood within the heart depends on the stage of compensation.

4. While compensation is maintained the heart contains a relatively normal amount of blood and is in a relatively normal position.

5. When compensation fails the amount of blood delivered to the heart is diminished, the heart becomes smaller and smaller until collapsed. The size of the heart varies inversely as the pericardial pressure. During this change the heart successively occupies positions varying from normal to that shown in Case I, or against the posterior wall of the pericardium.

6. The apex is in a normal position or displaced backward and slightly to the right; otherwise unchanged.

7. When the pericardial pressure is high, or when compensation is failing the signs should be triangular area of dulness, high pulse rate, perhaps pulsus paradoxus, low arterial tension, marked systemic venous congestion, and pronounced pulmonary symptoms.

LITERATURE.

1. Skoda: The heart sinks backward and downward. Quoted by Thayer. Johns Hopkins Hospital Bulletin, 1904. Vol. 15, p. 149.

Ewart: Apex beat unaltered or even lowered. Osler's Text-Book, p. 780.

Friedreich, Riegel, and Bauer: The heart is in a posterior position. Quoted by Zezschwitz. Munch. med. Wochenschrift, Vol. 48, p. 1348.

2. Schapozhnikoff, after relating his experiments and stating his conclusions, says: This tendency of the heart to remain near the anterior chest wall is due to the influence of its attachments to the basic vessels. If these vessels are ligated and the heart and its contents set free it will fall to the bottom of the pericardium. The heart does not sink by virtue of its specific gravity, as has been thought, but floats and is found to be above the pericardial fluid. Extract in the American Journal of the Medical Sciences, Vol. 131, p. 713, from Revue de Médecine, 1905, XXV, p. 789. This is a translation of the original in Russk. Arch. pat. klin. Med. 1. bakt., St. Petersburg, 1896, II, p. 75.

Frænkel: During a radical operation the heart projected into the opening, preventing the outflow of fluid, save during systolic contraction. Zur Lehre von der Perikarditis. Beiträge zur wissenschaftlichen Medicin und Chemie. Festschrift zu Salkowski. Berlin, 1904, p. 19.

Thayer, case II, says: "Friction rub—large heart near anterior thoracic wall—fluid posterior and to left." Johns Hopkins Hospital Bulletin, 1904, Vol. 15, p. 149.

Zezschwitz found the heart in an anterior position in one case. One of Pirogoff's cuts is reproduced on page 1351. Munch. med. Wochenschrift, Vol. 48, p. 1348.

3. Scott and Le Conte, in conclusion number four, say: "It is yet to be proved that the heart is pushed upward and backward in effusion." The American Journal of the Medical Sciences, Vol. 128, p. 447.

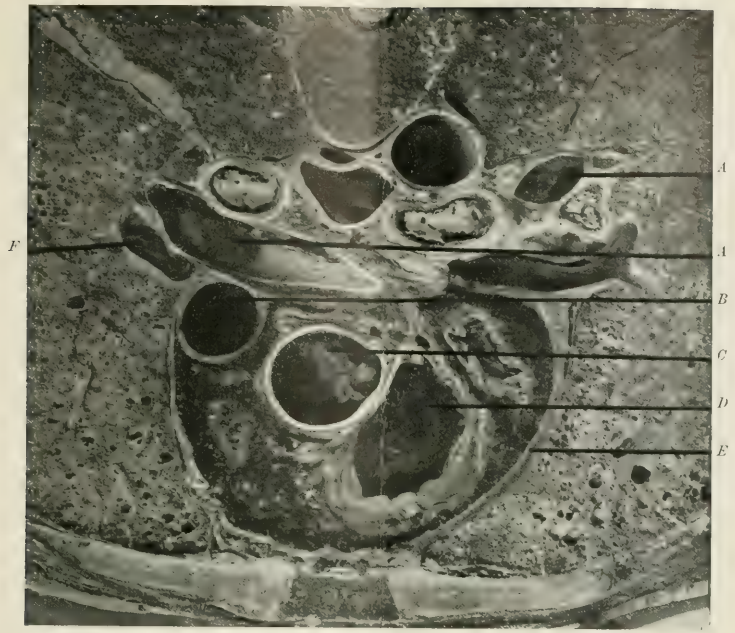

FIG. 5.

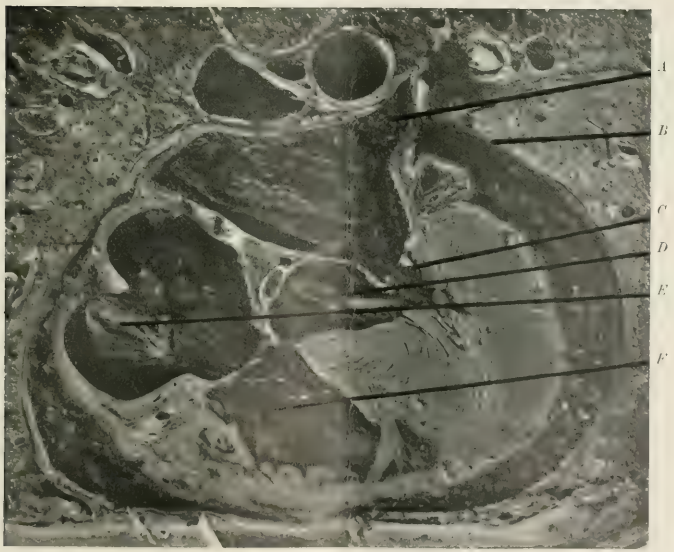

FIG. 6.

FIG. 7.

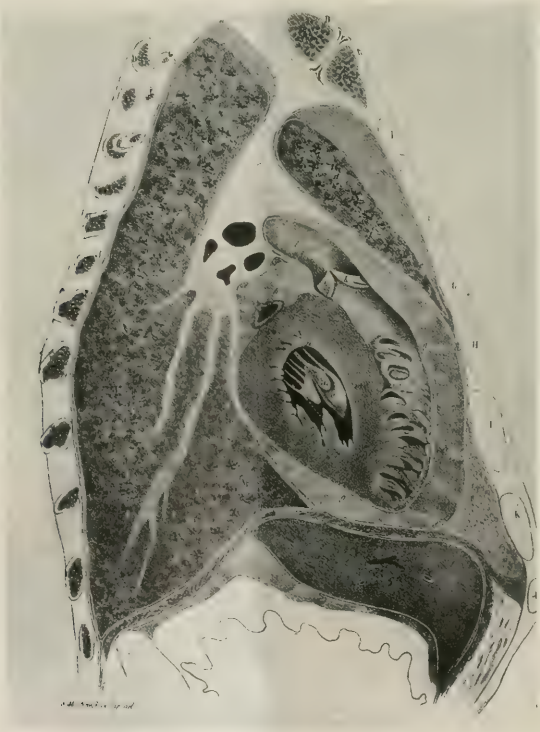

FIG. 8.

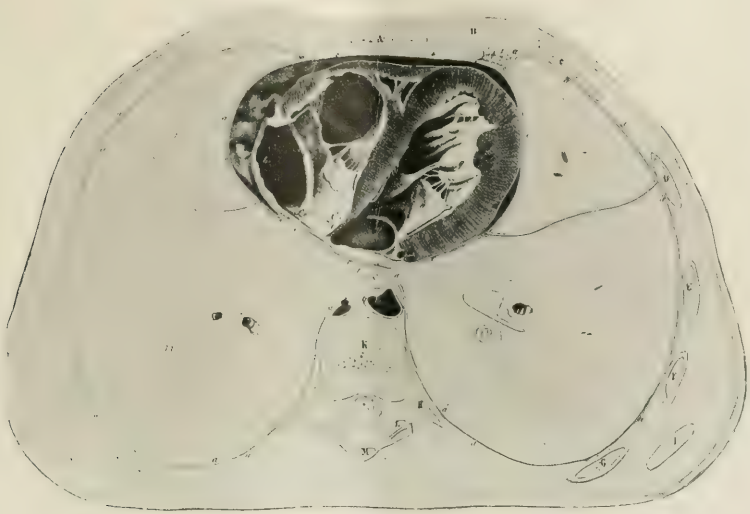

FIG. 9.

FIG. 10.

Romberg says that the heart rarely sinks in the fluid, and is separated from the anterior thoracic wall by a thick layer of fluid only in cases of very large effusions, p. 370; again, p. 375; the heart is seldom displaced to a marked degree. Lehrb. d. Krankh. d. Herzens, 1906.

Damsch says that the heart is in its normal position, but is not in contact with the anterior thoracic wall. Zeitschrift f. klin. Med., Bd. 38, p. 285.

Rendu and Ferrand say that the heart is retained in its normal position by the large vessels. Quoted by Thayer l. c.

Uslenghi says that the heart is in its normal position and not displaced downward. Semana Medica, Buenos Ayres, Vol IX, p. 286.

4. Warthin says that an early and persistent accentuation of the second pulmonic sound may be present. Osler, p. 780.

5. Gesammelte Beiträge, Bd. 3, p. 135.

6. Hensen, Deutsch. Arch. f. klin. Med., Bd. 67, p. 436.

7. François Frank, Gaz. hebd., 1877, No. 29.

DESCRIPTION OF FIGURES.

Pictures of Case I.

Fig. 1.—View of organs from left side. *a*, Parietal pleura; *b*, left lung; *c*, aorta; *d*, superior vena cava; *e*, pericardium; *f*, collapsed superior cava; *g*, heart; the heart is curved as shown in Fig. 3, so that this projection is much thicker than the heart really is; *h*, right auricle; *i*, collapsed inferior cava; *j*, inferior vena cava; *k*, right cupola of diaphragm; *l*, central tendon of diaphragm; *m*, left cupola of diaphragm.

Fig. 2.—Anterior projection of Case I. 1 and 10, lung borders; 2, aorta; 3, pericardial wall; 4, outline of collapsed heart; 5, tricuspid valve; 6, mitral valves; 7, collapsed portion of inferior cava; 8, diaphragm; 9, inferior cava; 11, collapsed portions of superior cava.

Fig. 3.—Transverse section of body showing flattened condition of the heart (*A*) and its relation to the pericardial wall (*B*).

Figures from Case II.

Fig. 4.—Anterior projection of Case II. *A*, lung border; *B*, jugular veins; *C*, superior cava; *D*, pericardial wall; *E*, aorta; *F*, superior cava; *G*, outline of the distended heart; *H*, mitral valve; *I*, aortic valve; *J*, right auricle; *K*, tricuspid valve; *L*, inferior cava; *M*, diaphragm; *N*, liver.

Fig. 5.—Transverse section of body just above the heart. *A*, pulmonary artery; *B*, superior vena cava; *C*, aorta; *D*, conus arteriosus; *E*, pericardium; *F*, pulmonary vein.

Fig. 6.—Transverse section through body showing the cavities of the heart and relationship of heart to pericardial wall. *A*, left auricle; *B*, pericardium; *C*, mitral valve; *D*, left ventricle; *E*, right auricle; *F*, right ventricle.

Fig. 7.—Transverse section of body showing lower portion of the pericardial sac and distended inferior vena cava. *A*, pericardium; *B*, lower portion of right auricle and inferior vena cava; *C*, coagulated effusion in pericardial cavity; *D*, lower portion of the left ventricle.

Figures Nos. 8, 9 and 10 are reproduced from Anatome Topographica, by Nicolao Pirogoff.

Fig. 8.—Shows a sagittal section of the body. The conus arteriosus, pulmonary valve, and a portion of the distended pulmonary artery well shown. The position of the heart in the pericardium is clear.

Fig. 9.—Transverse section of the body, under surface, the right heart is to left of picture. The cut shows a small pericardial effusion, the heart dilated and in a relatively normal position.

Fig. 10.—Transverse section of body, under surface of section shown, right heart to left of section. The heart is partially collapsed and separated from the anterior wall.

THE FETAL CIRCULATION THROUGH THE HEART.

A REVIEW OF THE MORE IMPORTANT THEORIES, TOGETHER WITH A PRELIMINARY REPORT ON PERSONAL FINDINGS.

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It would seem from the description in the various text books that the course of the blood through the fetal heart had been definitely settled. There are three major theories on the question which are reviewed in order of their general acceptance and inversely in the order of their appearance:

1. The first is the theory of Sabatier which appeared about the beginning of the 19th century. The blood entering the right auricle through the inferior cava was believed to cross (at least for the most part, Bichat's modification) through the foramen ovale to the left side. The more arterial blood in the left ventricle was expelled through the aorta, and in consequence of the origin of the large arteries to the head and front extremities, the more rapid growth, particularly of the head, was believed to be accounted for satisfactorily. A critical examination of this theory, which by the way, is the prevalent one at the present time, shows it to be physically impossible, morphologically inaccurate, and developmentally unnecessary. Physically impossible, because it would entail a distinct crossing of two currents under equal pressure within a distending chamber. Morphologically inaccurate, as Born pointed out, in that no such arrangement is found in the sauropsidian embryo, and still the head develops more rapidly, or even more strikingly in the human embryo where the leg buds, once they appear, develop more rapidly than the arm buds when on the Sabatier principle the reverse should be the case. Developmentally unnecessary in that a number of organs go rapidly from anlage to a relatively large size without being vascularized (kidney, testis). Nevertheless this theory is almost universally accepted and is pictured in practically all the textbooks on anatomy, embryology, and obstetrics.

2. The second theory was suggested by C. H. Wolff (1775),

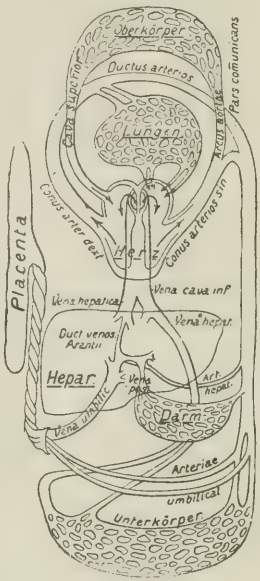
and although of earlier date, is a decided improvement on the foregoing. Wolff was able to appreciate a doubling of the orifice of the inferior cava or to put it in the words of Preyer (1884), "Es kann jetzt nicht mehr zweifelhaft sein, dass Casp. Friedr. Wolff Recht hatte, wenn er auf Grund seiner sehr sorgfältigen anatomischen Untersuchungen (1775) behauptete, der linke Vorhof erhalte gar kein Blut aus dem rechten Vorhof, sondern nur aus der unteren Hohlvene (und später den Lungenvenen), welche hinten an der Grenze beider Atrien, wie er fand, doppelt einmündet, so dass die linke obere Mündung nur dem linken, die rechte untere Mündung nur dem rechten Vorhof Blut zurführt. *Das Blut der beiden Vorhöfe kann sich also garnicht mischen,* wie auch Sabatier richtig betonte, und wie ich nach eigener Anschauung ebenfalls behaupten muss" (italics mine).

Preyer, however, still maintained that the head must receive a better quality of blood, although he believed the more arterial blood of the inferior cava to be divided equally to the right and left venticles. He argued that the pulmonary circulation was equal in quantity to that of the head and upper extremities and inasmuch as the lungs needed less oxygen, the return through the pulmonary veins must necessarily be purer than that of the vena cava superior. In consequence the blood in the left ventricle was more arterial than that in the right, and the result was similar to Sabatier's scheme, minus the disagreeable physical factor mentioned.

Preyer's findings were substantiated by his student, Ziegenspeck, in 1884. The latter presented an unique diagram, in which he represented the heart as two distinct hearts. After about twenty years (1905) Ziegenspeck has revived the theory once more and illustrated it by a figure which I have copied and which bears the title "Richtiges Schema des Placentarkreislaufs." It might be well to state that Ziegenspeck's article is detailed and carefully worked out, including the results of 36 injections into the umbilical vein of embryos.

Ziegenspeck really betters Preyer's work in that he eliminates the idea of a definite quality of blood and yet adheres to the quantity, believing therein to simplify the whole matter. The data furnished by Ziegenspeck might be questioned, because no matter how carefully the conditions are reproduced a dead animal is never the same that it is during life. The careful calibration of the various vessels is equally open to criticism because the amount of normal capillary resistance in the various vessels is probably different. There is at least no basis for assuming it to be the same.

Apart from this very general criticism, Ziegenspeck's figure itself is open for debate. Interpreted the figure means this: grant the contents of either ventricle to represent a volume equal to 5. Then inasmuch as the blood from the inferior cava is distributed equally to either ventricle, other return to the right auricle (vena cava superior, coronary sinus, and the smaller openings) must equal the pulmonary return. If this be true then the vena cava inferior returns 5 blood; the other return to the right auricle equals $2\frac{1}{2}$ and the pulmonary return equals $2\frac{1}{2}$. This is not imagination on the part of the writer, for it is made plain: "Das Blut des rechten Ventrikels, je gleiche Teile aus beiden Hohlvenen gemischt, ergiesst sich zur Hälfte durch den kleinen Kreislauf nach links. Das Blut des linken Ventrikels, $\frac{1}{2}$ aus der vena cava inferior. $\frac{1}{2}$ aus den Lungenvenen ergiesst sich zur Hälfte in den Oberkörper, zur Hälfte in die aorta descendens." The aorta descendens therefore receives $\frac{1}{2}$ of the blood from the right and $\frac{1}{2}$ of the blood from the left ventricle = 5.



It will be noted that three things are omitted from the diagram:

1. The coronary circulation which returns through the coronary sinus, but which I suggest as a modification, not a criticism. I take it by "obere Hohlvene" Ziegenspeck implies all orifices other than the vena cava inferior.

2. A certain amount of blood from the descending aorta returns through the superior cava (azygos circulation) and is omitted.

3. The lymph which passes through the walls of the branches of the aorta descendens (probably no small amount) is returned through the thoracic duct to the cava superior.

Returning to the amount of blood in the aorta descendens, if it is equal to 5, then 5 — blood must return through the cava inferior (subtracting the amount of azygos and lymphatic return). If each ventricle holds 5 and the blood of the inferior cava is equally distributed, then $2\frac{1}{2}$ + blood is returned by the superior cava (etc.) and the pulmonary veins respectively, but this cannot be the case, for then 5 — blood would pass through the descending aorta. With the major premise that no blood except that passing up the inferior

cava crosses to the left side, the scheme is rendered quite impossible.

The further statement of Ziegenspeck's: "Dass die linke Mündung der vena cava inferior enger ist als die rechte, ändert daran nichts," may be convincing to him, but it hardly covers the physics of the proposition, even if we grant the septal prominence actually does divide the orifice as stated.

The third theory is that of Harvey (1628), who believed that the blood of the superior and inferior cavæ mixed in the right auricle and that mixed blood passed through the foramen ovale. The theory appears quite logical if we but forget the time-honored idea that the head must receive a more arterial blood supply and the relations as they are pictured in the frog and the turtle.

It became evident that experiments must be carried on intra vitam in the embryo to eliminate all danger of artifact, and in consequence the pig embryo was chosen. The writer expresses his indebtedness to Kingan & Co., of Indianapolis, for the many courtesies extended.

The points outlined for investigation were the following:

1. Do both ventricles expel the same amount of blood?

2. In what proportion does the vena cava inferior return blood to each ventricle?

3. In what proportion does the vena cava superior return blood to each ventricle?

4. In what proportion does the sinus coronarius return blood to each ventricle?

5. In what proportion does the blood entering the lungs through the pulmonary artery return through the bronchial veins and pulmonary veins?

6. In what proportion does the blood entering the bronchial arteries return through the bronchial and pulmonary veins?

7. What is the proportion of blood returned to the left heart by the pulmonary veins?

8. In the frog does the blood from the two auricles remain separated in the common ventricle?

9. In the turtle does any of the blood entering the left auricle pass into the cavum pulmonale?

Owing to lack of facilities, question 1, 2, and 3 only will be answered definitely. Much research remains on the problem, and the writer takes the liberty to present this preliminary account because it throws light upon the crossing of the blood currents within the fetal heart. The manner in which the writer intends to obtain the desired results will, however, be touched upon.

The technique in a few words was this: Injection of the selected vein with a suspension of corn-starch granules in normal salt solution; recovery of the blood from the beating heart, both ventricles at the same time and under identical conditions; decolorization of equally diluted specimens and comparison of the two bloods for the number of starch granules. The details of technique are far more complicated to describe than the report warrants.

1. Do both ventricles expel the same amount of blood? This was assumed because of the adult relations, and while there were no grounds for believing otherwise, it was considered essential to substantiate the assumption. A ligature was slipped around the heart at the auriculo-ventricular groove and the ventricles together with their orifices tied off at the completion of ventricular diastole. This was accomplished successfully in two out of ten trials. Each ventricle was bled into a vial and the two sides compared. In both cases the blood was the same, and the question was considered as settled in the affirmative.

2. In what proportion does the vena cava inferior return blood to each ventricle?

Pigs nearly at term were left attached to the placenta and detailed precautions taken to eliminate false circulatory conditions; a quantity of cornstarch-salt solution mixture was injected into the umbilical vein with a hypodermic syringe. An incision was made into the chest, and the heart exposed, and both ventricles stabbed at the same time with identical pipettes. Pigs were rejected if any appreciable hemorrhage occurred or if the heart did not beat at least five times after the pipettes were introduced, or if the blood did not mount equally in both pipettes. Each paired sample was treated alike with ½ of 1% acetic acid to decolorize the red cells. The mortality was naturally great, but 25 paired samples were obtained of which eight were rejected, owing to flaw in dilution. The seventeen remaining paired samples were handled a pair at a time, as follows: each vial was shaken an equal number of times and a given quantity withdrawn and placed under cover. Comparison of the two sides resulted as follows: five were negative (no starch granules) and twelve positive (starch granules). In all twelve the number of starch granules appeared about the same, *i. e.*, they were so nearly equal that it was impossible to determine right from left except from the labels. This experiment proves beyond a doubt that Sabatier's theory is entirely incorrect, and substantiates the Wolff proposition or the Harvey theory.

To prove or disprove the one or the other, a second experiment was undertaken. If starch granules injected into the superior cava were recovered only from the right side, then the Wolff theory was correct and Harvey wrong. However, if the granules were found on both sides then Wolff was wrong and Harvey correct.

3. In what proportion does the vena cava superior return blood to either ventricle? The technique in this experiment was the same as above and would appeal to the reader as relatively simple. It was found extremely difficult to open the chest the full length without injury to the veins at the cervical limit of the thorax. Similarly it was difficult to inject the superior cava high up and inject only a drop or two to avoid undue pressure. Seven samples were finally obtained and submitted to the same requirements and tests. In the seven samples one proved negative (no starch granules) and six positive (starch granules). In four positive the granules were equal on both sides; in one more on the left than on the right, and one (labels unfortunately lost) more on one side than on the other. In both cases the excess

was easily 50%, and was attributed to some flaw in injection or in the recovery of the blood.

The point, however, was settled in the six positive tests. Starch granules injected into the superior cava did pass the foramen ovale, and apparently about equal amounts were found on the right and left side, thus proving conclusively that Harvey's teaching was right, that the blood of the two cavæ mixes in the right auricle and that mixed blood enters the foramen ovale, and showing that if Ziegenspeck, Preyer, and Wolff did find a double orifice to the cava inferior, it in no way inhibits a mixing of the two bloods.

The writer was surprised at the small amount of pulmonary return evidenced in that the starch granules were about equal on both sides, but attributes this to the collapse of the lungs and consequent increase of the capillary resistance and to pressure occasioned on the pulmonary veins by manipulation of the heart. This note will show the difficulties in the remainder of the problem.

The results show that all the organs of the body receive about the same quality of blood, and that the quantity is certainly not the rule laid down by Ziegenspeck. The diagram resulting from this investigation is quite evident, and when published will include the coronary, bronchial, azygos circulations and the lymphatic return.

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TWO CASES OF TYPHOID FEVER WITH INTERESTING BLOOD CRISES.

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Case I. *Summary.*—A case of typhoid fever, admitted on the 17th, and with death on the 30th day of disease; blood crisis; a period of hypothermia associated with numerous small intestinal hæmorrhages.

W. C., colored, aged 27 years, a fireman, was admitted to Ward M of the Johns Hopkins Hospital October 6, and died October 19, 1906. General number 56,517.

He complained of "dumb chills, loss of sleep, headache, and feeling out of sorts."

The family history was perfectly negative. His parents, four of five brothers, and eight sisters were all alive and well. One brother died when a baby.

Past history.—When a child he had measles, mumps, chicken pox, and whooping cough. He never had had diptheria, scarlet fever, chorea, any form of rheumatism, typhoid fever, pneumonia, or pleurisy. He was once treated for chills and fever, but had never been ill in bed before the present illness. He denied all symptoms suggesting eye troubles; he had a discharge from one ear when a child. He was not subject to colds and had no gastro-intestinal symptoms. He had had gonorrhoea and evidently lues also. He denied having used tobacco and claimed to have always been very temperate in the use of alcohol. His work was not heavy.

The present illness began September 16, on which day he awoke with a headache and general malaise. Although this continued, he worked until September 19. During this time he was quite constipated, and took considerable medicine to relieve this symptom. On September 19 he had to stop work because of the malaise and a very severe headache. That afternoon he had a "dumb chill." These "dumb chills" occurred every afternoon for several days. He described them as periods during which he felt cold. They were not shaking chills. He remained in bed for the next few days, feeling very ill, with poor appetite, headache, weakness, insomnia, and later diarrhœa. On the night of September 29 he awoke in a hot fever, which was followed by a drenching sweat. The next day he came to the Outpatient Department, and quinine was prescribed although on careful examination no malarial parasites were found in the blood. He had no more chills, but he grew progressively weaker, could not sleep, and had a severe diarrhœa of seven or eight movements a day, but had absolutely no pain in the body and no tenderness in the abdomen. He often belched, but had no nausea and no vomiting. He was admitted to the ward October 6, probably the seventeenth day of his illness.

Physical examination.—The patient was a well built, well nourished negro. He lay comfortably on his back in bed. The scleræ were a little yellow, otherwise the eyes were negative. The ears and throat were both negative. The mucosæ were rather pale, the tongue was covered by a thin white fur.

There was general glandular enlargement; the glands of the posterior triangles of the neck, of the axillæ, of both inguinal regions, and the epitrochlears were all enlarged.

The lungs were negative on auscultation and percussion. The heart impulse was in the fourth and fifth spaces, maximum in the fourth, 7 cm. from the mid-sternal line. There was no thrill at apex or base. The deep cardiac dullness extended 10 cm. to the left in the fourth, 2.5 cm. to the right in the third interspace, and above to the lower border of the second rib. The heart sounds were clear, with a relative accentuation of the aortic second sound.

The abdomen was natural in appearance and its movements free. There was some gurgling in the right iliac fossa. No masses were felt, there was no muscle rigidity and no pain on deep palpation.

The relative hepatic dullness began above at the sixth rib in the right mammary line and extended just to the costal margin. Its margin was not palpable. The firm margin of the spleen was easily palpated. The genitalia were negative. There was no œdema of the ankles. The deep reflexes were normal.

The pulse was 80 to the minute, small in volume, of low tension, regular in force and rhythm. The arterial wall was not especially thickened.

Blood examination.—Red cells, 3,896,000; leucocytes, 6800. The red cells were of quite uniform diameter, and of rather pale color. No malarial parasites were found, and no pigmented leucocytes.

Polymorphonuclear neutrophiles	88.8%
Small mononuclears	6.4
Large mononuclears	1.4
Transitionals	2.2
Unclassified	1.2

On October 8, the leucocytes were 4, 620.

October 10. Blood examination: Red cells, 3,752,000; hæmoglobin, 55 per cent; leucocytes, 4,200.

October 11. This morning the stool following a soap-suds enema was pinkish in color and contained three or four small blood clots. The total amount of blood could not have exceeded 15 ccm. This slight hæmorrhage was followed by no symptoms. The temperature, however, dropped from 103° at 4 a. m. to 101.2° at 6 a. m., but in two hours had risen again to 103°. The pulse rose slightly (from 92 to 104) during this drop of temperature, but at 8 a. m. was again 94. Twelve hours later the stools consisted mainly of fluid blood with a few clots, about 200 ccm. in all. We suspected this to be a portion of the same hæmorrhage evacuated earlier.

October 12. A sudden abdominal pain led us to fear that a perforation might have occurred, hence the leucocytes were to-day frequently counted.

10.30 a. m.	11,800
1.15 p. m.	10,300
2.15 p. m.	11,900
3.25 p. m.	13,900
7 p. m.	13,500

At 2 p. m. a third small hæmorrhage was evacuated, consisting of about 200 ccm. of dark fluid and a few small clots.

The temperature on the day before at 8 a. m. was 103°. It fell steadily, reaching 96° at 6 a. m. on this day, and varied from 96° to 98° until 12 m. three days later, October 15, when it rose again. The pulse during that time varied from 94 to 130 and the respirations from 24 to 32.

October 13. The patient looked very ill. He lay with his mouth open and limbs tremulous; the tongue was protruded with difficulty. The pulse was dicrotic and averaged about 112. There was marked pallor of the mucosæ. The abdomen was rather full and rigid, but there was no point of tenderness on pressure. The heart sounds were clear and of normal relative intensity.

Blood examination.—The red cell count was 2,104,000. The stained specimens showed some poikilocytosis and a good many microcytes. Many red cells were polychromatophilic. Hæmoglobin, 30 per cent; color index, 0.7; leucocytes, 16,940. (This includes the nuclei of about 65 nucleated reds.)

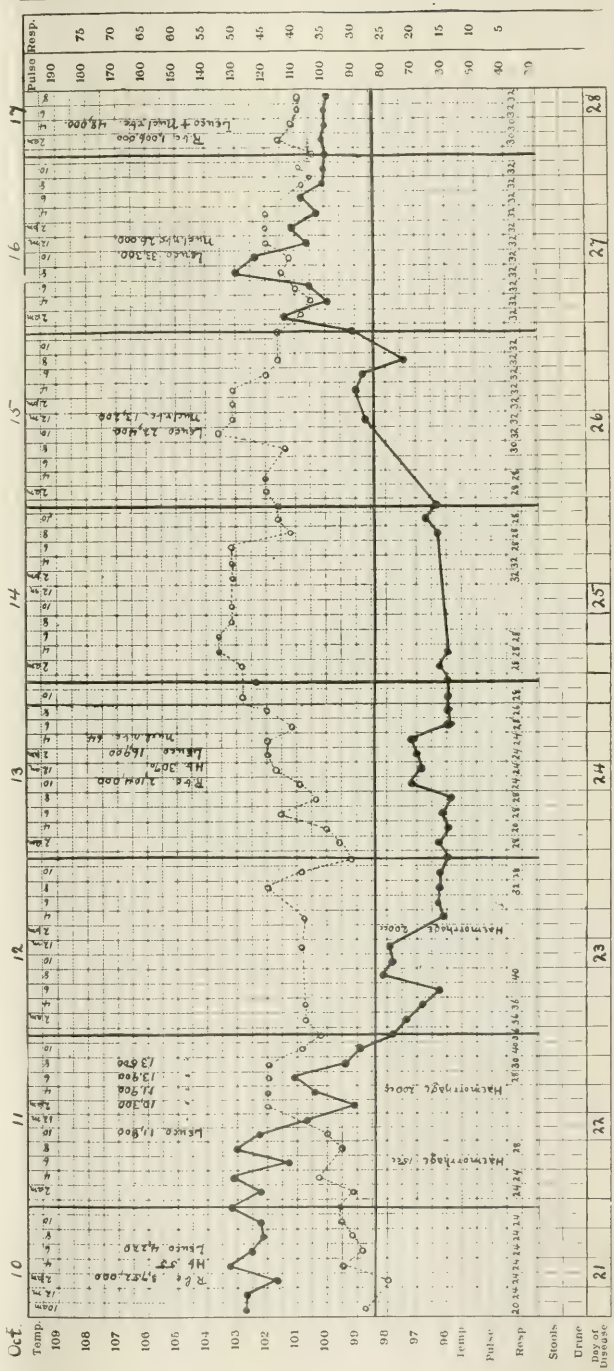
Polymorphonuclear neutrophiles	76.8%
Small mononuclears	16.4
Large mononuclears	3
Transitionals	3
Myelocytes (neutrophiles)	0.2
Unclassified	0.6

No eosinophiles and no mastzellen.

While counting 500 leucocytes two normoblasts were found.

October 15, 9 a. m. The patient looked more ill. The tongue was dry and glazed, there was considerable tremor of the lower jaw, and some subsultus of the arms. The abdomen now was retracted to a remarkable degree. It was rather rigid, but not tender on palpation. The pulse was 124 to the minute, the heart sounds were clear with the aortic second loud. The leucocytes were 30,700 at 2.30 p. m. Temperature subnormal.

4.45 p. m. The patient was very dull and drowsy. He denied that he had any pain. The neck was not stiff. There was no nausea or vomiting, no pain on defecation or micturition. The lungs and heart were both negative. The abdomen was a little fuller than in the morning yet was by no means distended. The



W. C. Typhoid fever; hæmorrhages; hypothermia; megaloblastic blood crisis.

abdominal muscles were held rather stiffly, but there was no local tenderness, no muscle rigidity, or muscle spasm. There was no dullness in the flanks. The liver dullness just reached the costal margin. The lower zone of the abdomen moved on deep breathing very little. Rectal examination was fairly negative, although pressure toward the right caused more pain than toward the left.

The leucocyte count at 5.30 p. m. was 34,600, and at 8.30 p. m. was 37,400.

9.45 p. m. The patient's condition seemed worse. There was more tenderness on the left side of the abdomen and a few suspicious dry râles under the left costal margin. The facial expression was somewhat drawn. The pulse was better than this morning, the aortic second sound was still clear. A typhoid perforation was suspected, and an exploratory laparotomy strongly urged.

10 p. m. Prior to transferring the patient to the surgeons a complete examination was made. This we copy in full.

"On October 11 the temperature fell from 103° to 96.2°. Since then, until this evening, it has not been above 98°, and seldom even 97°. On October 11 the pulse rose from 98 to 120 and since then has not been below 100. This evening the temperature has risen to 99.9° and the pulse to 132. Since October 11 the respirations have varied from 24 to 28; this evening they are 32 per minute. Since admission he has markedly emaciated, is very weak, often irrational, and now is held by a restraining sheet. His arms are twitching. The hands and feet are very cold. The pupils are almost pin-point in size. They react slightly to light. There is no stiffness of the neck. The interior of the mouth is dry, there are sordes on the teeth. The alae nasi do not dilate on inspiration. The posterior cervical, the axillary, the epitrochlear and the inguinal lymph glands are all enlarged and firm.

"The pulse is 142, regular in force and rhythm, small in volume, and low in tension. There is marked arterio-sclerosis.

"*Chest.*—The right front and axilla are hyper-resonant on percussion, and negative on auscultation. The left front is less hyper-resonant than the right. At the left base behind the breath sounds are scarcely heard. On deep breathing they are slightly bronchial in character. The voice sounds at the base are not nasal; the vocal fremitus is there easily felt. The heart sounds are best heard under the left nipple, are clear at apex and base; the pulmonic second is accentuated.

"The abdomen is scaphoid; the respiratory movements are absent below the navel, even on deep respiration. Shadows of loops of bowel are distinctly seen to descend on inspiration.

"*Liver.*—The relative hepatic dullness begins at the lower border of the sixth rib and extends to just below the costal margin. The edge of the liver is just felt. The spleen is not felt, nor is the splenic dullness increased. The abdomen is everywhere soft. There is no local muscle rigidity, no muscle spasm, only a slight tenderness on palpation over the lower extremity of the right rectus muscle, and this is inconstant. In the right iliac fossa is distinctly felt a tumor suggesting a mass of lymph glands at the base of the cæcum. The sigmoid flexure can be rolled under the finger. There is tympany in the flanks.

"*Extremities.*—The shins are clear; there is no œdema of the ankles, no paralysis of the leg and no Kernig's sign. The knee kicks are active; there is patellar clonus. On plantar stimulation there is flexion of the great toes. The deep reflexes of the upper arms are active and there is also marked myoedema. The patient has had no nausea, no vomiting, or hiccough. The bowels have not moved since the last hæmorrhage on October 12. The total of the hæmorrhages has certainly been less than 500 ccm. of blood. There is no tenderness in any joint and no local swelling of the extremities. The Widal reaction tried to-night is very suggestive, but not positive.

"*Blood.*—The leucocytes have risen from 4000 on October 10 to 38,000 this evening. The fresh blood specimen shows marked anæmia. The red blood cells must be very susceptible to injury, since most of them are crenated or otherwise injured, and yet the technique used was careful. A remarkable feature is the large number of nucleated reds, especially megaloblasts and intermediate forms. There are many normoblasts. Many of the nucleated reds have fragmented nuclei. The red blood cells vary markedly in size, but none have a sausage or battledore shape. The majority of the leucocytes are finely granular polymorphonuclears. One typical finely granular myelocyte is seen. An approximate leucocyte count made with the high power showed that many of the nucleated cells counted as leucocytes were red cells and some of them typical megaloblasts. The condition simulates a primary anæmia, perhaps an acute leukæmia with a blood crisis. If the case is typhoid fever, the patient is having a crisis of a most unusual character. Operation not advised."

A most careful study was then made of smears taken during this examination. The total count of nucleated cells was 35,600 per cmm. While making a differential count of 511 leucocytes, there were found 90 normoblasts, 37 intermediates, 9 megaloblasts, and 4 free nuclei. The leucocyte count must have been, therefore, about 28,000, and that of the nucleated reds 7600 per cmm.

Differential count:[1]

Polymorphonuclear neutrophiles	89.43%
Myelocytes	0.97
Small mononuclears	6.26
Large mononuclears	1.18
Transitionals	0.97
Unclassified	1.18

October 16. The patient appeared better and responded well to questions. The alae nasi dilated with inspiration. Respirations were quick, 32 to the minute. The pulse was dicrotic and 110. The temperature had risen to 103°. The mucous membranes were very pale; that of the throat was white and parchment-like, covered with dried secretion. The tonsils were not enlarged. The lungs were negative. The abdomen was still scaphoid, and scarcely moved below the umbilicus. Coils of intestine in active peristalsis were seen around the umbilicus. There was no muscular rigidity and no pain on deep palpation. The flanks were tympanitic. The liver dullness reached just to the costal margin.

The leucocyte count was 59,300, but of these only about 33,300 were white cells, the rest were the nuclei of red cells, for in counting 520 leucocytes there were found, of perfect normoblasts 103; normoblasts with fragmented nuclei 50; microblasts 1; intermediates 30; megaloblasts 15.

Polymorphonuclear neutrophiles	82.3%
Myelocytes	6.46
Small mononuclears	7.79
Large mononuclears	2.28
Unclassified	1.14

No eosinophiles and no mastzellen.

October 17. The patient was distinctly better. The pulse was 104 to the minute, soft and better in quality. The pulmonic second sound was louder than the aortic.

Red corpuscles	1,006,000
Leucocytes	48,000

October 18. The patient now in a muttering delirium.

October 19. Leucocytes 11,340.

[1] All of these counts we owe to Dr. W. D. Gatch, then a clinical clerk on this ward. Ehrlich's triple stain used.

Polymorphonuclear neutrophiles	89.4%
Small mononuclears	9.4
Large mononuclears	0.2
Transitionals	0.2
Unclassified	0.8

While counting 500 cells, 40 normoblasts and 3 intermediates were found.

October 19. The patient died to-day at 4.30 p. m., evidently of exhaustion. He had emaciated extremely.

A trace of albumin was constantly present in the urine, and a few hyaline and granular casts on some examinations. The Diazo was negative. The stools were negative.

Autopsy, No. 2781, October 20, 1906. Fourteen hours post-mortem.

Anatomical diagnosis.—Typhoid fever; ulceration of ileum; acute splenic tumor with anæmic infarctions, and acute perisplenitis; red bone marrow; necrosis of liver and marrow.

(The autopsy notes given here are considerably condensed from the original.)

The body is that of an emaciated negro man, 176 cm. in length. Decubitus ulcer over sacrum, and ulcer on skin of scrotum. The peritoneal cavity is drier than normal, its surfaces are glistening. The intestine is markedly collapsed, and its coils lie away from the spinal column, so that the anterior abdominal wall rests against the back-bone. The spleen is somewhat enlarged; the liver extends below the costal margin. The pleural cavities are free from fluid and adhesions. The pericardium is smooth; its cavity contains no excess of fluid. The heart is not enlarged. The endocardium, valves, and muscular wall are normal. The lungs are rather moist and a good deal of frothy liquid can be squeezed from them, but otherwise they are negative. There is no consolidation anywhere. The spleen weighs 210 gm., and measures 12 x 10 x 5 cm. The surface is rendered uneven by irregular firm projecting nodules, varying in size from 2 mm. to 3 cm. These areas are elevated and quite firm. They are yellowish-white, some with white dots and streaks, and are outlined by a red halo. The remainder of the spleen is fairly firm, and is of a dark grayish-red color. The whole of the spleen is covered by a thin layer of fibrin which is perhaps thickest over the projecting areas, and can readily be removed. On section the firm nodules are seen to be dry, elevated above the cut surface and yellowish-red in color. They are opaque, dull, and dry looking, and show dimly the architecture of the spleen. They are roughly quadrilateral on section and the reddish-yellow central portion is outlined by an opaque, pale yellow line, which is further separated from the remaining splenic pulp by a red line. These nodules are all superficial and extend to the surface. The splenic pulp in general is grayish-red and swollen. The Malpighian bodies and trabeculæ are fairly well seen. In the neighborhood of the opaque yellow areas there are other irregular patches which look dull and dry, and are slightly firmer and red of only a slightly paler hue than the rest.

The stomach, pancreas, duodenum and gall bladder showed nothing worthy of note.

Intestines.—The ileum throughout its upper part is normal looking. There are some Peyer's patches high up which seem swollen and have the appearance of the elevated Chinese letters seen on a Chinese coin. The elevation is in streaks only. Lower, the Peyer's patches are thickened, but not to a very great extent, and rather smooth looking. Near the ileo-cæcal valve there are several ulcers, which vary in size from a few millimeters to almost two centimeters in diameter. Their edges are rather precipitous, but they are not deeply congested. One near the ileo-cæcal valve is about 8 mm. in diameter and is very deep, laying bare the muscle layer. A slight thickening is visible on the serosa opposite. The other patches in the neighborhood are swollen, but not definitely ulcerated. In all there are only three or four small ulcers. The mucosa of the colon is normal looking. The mesenteric glands opposite the ileum are enlarged, pale yellowish in color, and rather firm. The retroperitoneal glands are not enlarged. No definite hæmolymph glands could be recognized. The bladder, rectum, genital organs, and thoracic duct presented nothing of importance.

The kidneys are of about normal size, and weigh 300 gm. The cortex is 7 mm. in thickness. They appear normal on the surface and on cross-section.

The adrenals, aorta, thyroid, and parathyroids all appear normal.

The liver is of normal size. Its surface and cross-section appear normal. No focal necroses were seen macroscopically.

On microscopical examination, the heart showed nothing worthy of note.

The lymph glands in the mesentery show some sclerosis. There are a few large phagocytic cells in the sinuses. There are numerous colonies of bacteria, apparently bacilli, scattered in the tissue. These are also seen in the intestinal wall.

Spleen.—There are well defined anæmic infarcts of characteristic histological structure. In these necrotic areas there are also masses of bacteria. The spleen in general is rather hyperæmic. The venules seem to be filled with a homogeneous hyaline material which stains a grayish-pink and which makes the splenic substance quite solid in places. In other patches the venules contain blood. There are a very few cells containing red corpuscles.

Liver.—There are many definite focal necroses in which the liver cells are lost, and the invasion of polymorphonuclears and mononuclear cells has taken place. Often the outline of the dead liver cell can be made out. The necroses are scattered throughout the lobule, frequently appearing in the middle zone. At the surface of the liver there is one large necrotic area into which no leucocytes have as yet wandered. The capillaries here seem filled with hyaline thrombi.

Marrow of femur.—Sections of bone marrow taken from the femur, and hardened in Zenker's fluid, show a patchy hyperplasia of the marrow cells. Some areas show fat cells only, but in such areas the lymph spaces are widely dilated, and full of a finely granular, pink-staining coagulum. The capillaries throughout are dilated. Areas of focal necrosis are seen, but they are of small size and their fibrin does not take a very deep eosin stain. These areas are found among the fat cells as frequently as in the patches of hyperplasia. The striking feature of the cellular marrow is the great number of nucleated cells, both normoblasts, megaloblasts and intermediate forms. These cells occur as a rule in clumps or islands (Bunting) which are very striking. Some of these islands show as many as 15 or 25 nucleated red cells crowded rather closely together and in the center of such islands one may see a few indifferent marrow cells. The nucleated red cells are less conspicuous in the capillaries and their nuclei smaller and more pyknotic.

Non-granular mononuclears are not numerous and are quite inconspicuous, less numerous even than the nucleated red cells. The small mononuclears occur in small clumps, but none of the large lymphatic nodules described by Longcope are made out.

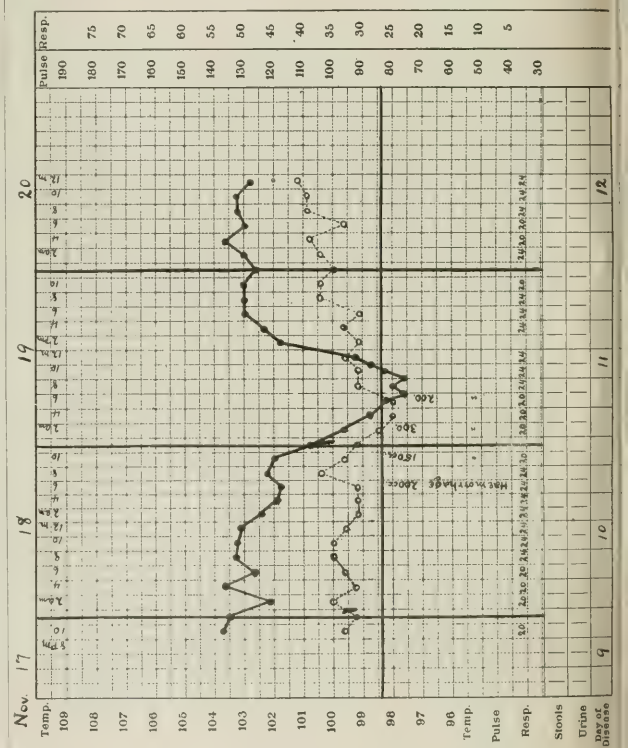
Myelocytes are very conspicuous, being the predominant cells, but the polymorphonuclear leucocytes are relatively few, and evidently most of them have been swept out of the marrow.

Eosinophile myelocytes and leucocytes are easily found. Not infrequently they are found in clumps of from 3 to 9 cells. The bone marrow giant cells are found in small numbers. They are usually of small size, shrunken, and only occasionally show pseudopodia. Large phagocytic cells, situated usually in the capillaries, are found only after prolonged search. They are large mononuclear cells with deeply eosin-staining granular protoplasm, which may contain red blood cells or nuclear fragments. No phagocytes containing coarsely granular yellow pigment were seen.

Cultures made from the spleen, splenic infarct, femur marrow, and vertebra marrow gave pure cultures of Bacillus typhosus. That from the rib marrow, Bacillus typhosus and Bacillus lactis ærogenes.

Our case was, then, one of typhoid fever admitted on the 17th day and with death on the 30th day of the disease. Clinically it was quite characteristic, but the positive diagnosis of typhoid fever was not made until autopsy. Four Widal agglutination tests were reported negative according to our standard, which is a very rigid one, since it demands good agglutination and practically complete cessation of motility in a one-to-fifty dilution, and at the end of one hour. The agglutination at this dilution was good in all four tests, but in each there remained a few motile bacilli. At autopsy four small ulcers of Peyer's patches, were found, which on microscopic examination were typhoid in character. Bacillus typhosus, however, was cultivated from the organs, and this settled the question.

One feature of this case which especially interested us was the period of hypothermia which occurred in association with a few very small intestinal hæmorrhages. On the 22d day of the disease the temperature was 103° F. It began to fall, reached on the following day 96.2° F., and remained at about 96° F. for three full days. Preceding and during the first thirty-two hours of this fall there were passed three stools, which possibly contained 500 ccm. of blood altogether, but we think this is too high an estimate. At the same time the pulse rose from a mean of 95 to a mean of about 120. For the temperature to fall during a hæmorrhage is not uncommon, and yet in a majority of cases, if the temperature chart be shown to a doctor, he cannot pick out the day of the hæmorrhage. In a young, strong patient a sudden hæmorrhage of about one litre of blood is often accompanied by a drop of temperature to a subnormal point. If this hæmorrhage be rapidly evacuated the temperature returns promptly to its previous high point, reaching it in roughly twenty-four hours from the time it began to fall. Contrary to the usual text-book statement, the pulse often does not change at all, but remains low, and even may drop, as in the case of a patient in the hospital at about the same time, a portion of whose temperature curve we give on Chart II. The rate of respiration also shows no change. The delirium often disappears and the patient is for a time mentally much clearer. Sometimes this clearing of the sensorium is accompanied by a very definite feeling of apprehension. There is no pain, no local sensations whatever, but suddenly the patient becomes mentally clearer and is afraid something dreadful is about to occur, but what he does not know. The temperature begins to fall. Then one may be on the lookout for a stool or stools containing blood in large amounts. The apparent temporary improvement in the case explains beautifully the logic of bleeding fever patients, so much in vogue a few decades ago. What more can one ask as the result of a therapeutic measure than that even for one day a delirious fever patient become mentally clear, his temperature fall to normal and the pulse not increase in frequency.



But the case we here report belongs to a different, and not rare class (Chart I). The temperature falls to a low point and remains there for some time. The pulse may rise and the patient may appear even more toxic than before. And yet the haemorrhages are small, often multiple, with the aggregate amount of blood lost much less than in the cases of the former group.

We do not know how to explain the differences. It may be the patient is very weak, emaciated, and almost at the limit of his strength. Such was the case of this patient, but not of another patient in the ward that same season. This was a strong young man, twenty-three years of age. The temperature was already beginning to approach the normal line, when, on the twenty-seventh day of his fever, he had an intestinal hæmorrhage of not over 200 cc. of blood. A period of hypothermia of thirty-six hours followed. It may be a feature of hæmorrhages late in the disease, and after defervescence has begun. It may be that in the case of one sudden profuse hæmorrhage the blood is passed at once, and so there is much less reabsorption of the blood and its decomposition products than when there are multiple small hæmorrhages which remain in the bowels much longer. That is, the whole picture may be more a toxæmia than the result of the loss of so much blood, and of whatever toxins it may contain.

The feature of this case to which we wish to call especial attention is the remarkable blood crisis which occurred during and after this period of hypothermia.

On the 21st day of the disease the leucocyte count was 4,200. On the 22d day the temperature began to fall. On this day the leucocytes were not counted. On the 23d day, with the temperature subnormal, the counts were 11,800; three hours later 10,300; one hour later 11,900; in another hour 13,900; and four hours later 13,500; all practically the same count. On the following day, the count was 16,900. On the 20th day no count. On the following day they had risen; 30,700, 34,600, 37,400, and 35,600 being the counts made at regular intervals. We know, however, that the count 35,600 included the nuclei of 13,200 red cells, and so the white count was 22,400. Without doubt the other counts need a like correction. During the hours of these counts, the temperature was rising. On the 27th day, with the temperature 102.4° F., the leucocyte count was 59,300. Of these cells, however, only about 33,300 were leucocytes, and the remainder were the nuclei of red blood cells. The following day the count was 48,000. The next count was made on the 30th day of the disease, four hours before death. It was 11,300, of which about 10,400 were white, and 900 the nuclei of red cells. Parallel with this rise of the white cells from 4200 to 33,300 and the fall to 10,400, the nucleated reds appeared and rose to at least 26,000, then fell to about 900 per cubic millimeter. Of the 7,600 nucleated reds present on the 26th day of the disease, at least 40 per cent were megaloblasts and intermediates; of the 26,000 present the following day, about 22 per cent were these cells. It was, therefore, a megaloblastic blood crisis. During this crisis, often interpreted as unusual activity of the bone marrow, there was a polymorphonuclear neutrophile leucocytosis, with also 6 per cent of neutrophile myelcocytes, but the eosinophiles were conspicuous by their absence.

We have given elsewhere[2] our opinion of blood crises. We believe that while they are splendid evidence of the struggle the bone marrow is making, the chances are they will not accomplish much in raising the red blood count if the marrow is reduced to the necessity of pouring the larger nucleated cells into the blood stream. This case is a good illustration of this point, for the count on admission was 3,896,000, and four days later, on the 21st day of the disease, it was 3,752,000. On the 24th day it was 2,104,000; and on the 28th day, 1,006,000. That is, the crisis occurred during a rapidly developing anæmia.

It is impossible to give the reason for this crisis in the present state of our knowledge. That it bore a direct relation to the hæmorrhages we do not believe, since it began before and continued after these. We are tempted to bring it into relation with the infection of the bone marrow, for at autopsy a pure culture of Bacillus typhosus was obtained from this tissue, and histologically the bone marrow showed widespread necrotic lesions. This theory is tempting, and is not new, for some cases called acute leukæmia are thus explained. These are cases of rapidly fatal acute infections, with a marked anæmia and a leucocytosis, polymorphonuclear in character, yet with a fairly high percentage of mononuclear cells, both granular and non-granular. From the bone marrow of a few of these cases, pure cultures of pathogenic bacteria have been obtained.[3] It is tempting to regard this case as one of typhoid fever with especial localization of the infection in the bone marrow, causing widespread death of this tissue, a resulting progressive anæmia, and a very vigorous, yet futile effort of the remaining functioning tissue, as shown by the blood crisis, to stem the ebb tide. But how seldom are cultures made from the bone marrow of persons who have died from typhoid fever, and how very seldom is a systematic histological study made of this tissue.

Case II. *Summary.*—A case of typhoid fever with death during the second week. Blood crisis.

E. H., 47 years of age, a fireman, was admitted to Ward E of the Johns Hopkins Hospital September 7, and died September 10, 1907. General number, 60,667.

He complained of "hæmorrhages and weakness."

His family history was quite negative. His past history was also quite negative. He had always been strong and well. Only once had he been confined to his bed, and that was years before, when he had some form of "rheumatism." He never had typhoid fever, pneumonia, pleurisy, or malaria, and denied all children's diseases. He was slightly jaundiced ten years ago.

Until two years ago his digestion had been very good, and until the present illness he has never vomited blood, or passed any

[2] Emerson. The Blood in Pernicious Anæmia. Johns Hopkins Hospital Bulletin, 1907, xviii, 51.

[3] Emerson. Acute Leukæmia. Johns Hopkins Hospital Bulletin, 1907, xviii, 71.

dark stools. During the past two years any indiscretion in diet had caused some gastric pain and a diarrhœa, but nothing more. No cardio-respiratory symptoms were complained of. For one year he had noticed slight swelling of the ankles, but no increased frequency of micturition. He denied all symptoms on the part of the special senses. He used tobacco; and alcohol in great moderation, only about a dozen glasses of whisky a year, but never beer. He worked as a locomotive fireman.

The present illness he dated back to September 1, although his friend stated that he had noticed that the patient had looked pale and sick for a week before that. On September 1 he noticed that his stools contained large black blood clots, and since then the stools had been very black and tarry, but had never contained fresh blood. Two days before this he had taken a dose of calomel. On September 1 he also vomited about a cupful of bright red blood, and again, about the same amount September 5.

He had lost strength rapidly during this week.

On admission, September 7, the patient was found to be a stout man, weighing between 200 and 210 pounds. He was lying flat on his back, and complained of no pain or discomfort. His skin and mucous membranes were very pale. The respirations were 28, and the pulse 120 to the minute. The scleræ, pupils, pupillary reflexes, and movements of the eyeballs presented nothing of importance. There was no jaundice.

The throat was negative, the tonsils not enlarged.

There was no glandular enlargement.

The lungs were typically emphysematous.

The heart presented nothing of importance. It was neither hypertrophied nor dilated.

The abdomen was practically normal. The spleen could not be felt. (The patient was stout, and held his abdominal walls rigidly.) The relative hepatic dullness began at the 6th rib and descended to just below the costal margin, but its edge could not be felt (perhaps for the same reason that the spleen was not). There were no dilated veins on the abdomen.

There was slight œdema of the ankles. No purpuric spots were seen anywhere on body.

There were 1,300,000 red blood corpuscles, and 85,000 leucocytes per cubic millimeter. Hæmoglobin, 25 per cent (Sahli's hæmometer). The red cells were rather pale, and many of them on staining were polychromatophilic. The blood platelets were very numerous. Differential count. (Ehrlich stain; Dr. Clough.)

In counting 530 leucocytes, 88 normoblasts, 7 intermediates, and three megaloblasts were found. There were, therefore, about 71,500 leucocytes, and 3500 nucleated reds per cubic millimeter.

Polymorphonuclear neutrophiles	74.5%
Neutrophile myelocytes	8.8
Cells intermediate between above two groups	6.3
Large mononuclears	6.2
Small mononuclears	3.3
Eosinophiles	0.2
Mastzellen	0.
Unclassified	0.7

September 8. No apparent change.

September 9. Nucleated blood cells, 90,000 per cmm. No purpuric spots, no enlargement of the lymph glands could be found. The respirations and pulse now become more rapid.

September 10. The patient died early this morning.

The temperature while in the hospital was 99.6° on admission, but rose at once to 103°, and after that the extremes were 101° and 104.4° F. The pulse varied from 100 to 146. The respirations, at first about 28 to the minute, were later from 40 to 44.

He passed while in the hospital about 1200 cc. of urine a day—that passed on admission was clear, but on the day of death it contained a trace of albumin and a few hyaline and finely granular casts. The five stools were tarry.

In blood cultures, made September 9 by Dr. Beall grew later a pure culture of Bacillus typhosus.

Most unfortunately no autopsy was allowed.

This case came to us with the diagnosis of cirrhosis of the liver, rupture of œsophageal varices, and secondary anæmia. We found very little evidence of cirrhosis of the liver, and diagnosed it as one of the cases now often included in the acute leukæmias, meaning by this an infection with this unusual blood picture. The discovery of Bacillus typhosus in the blood leaves no doubt that it was a case of this infection. It is very possible that the man had cirrhosis of the liver, and that the hæmatemesis and melæna were due to a bleeding œsophageal varix. We cannot say. The interest for us lies in the effect of hæmorrhages in typhoid fever on the blood picture. The blood picture of Case II resembled that of Case I. In both there was a severe anæmia, a very high leucocytosis, with a fairly large number of typical neutrophilic myelocytes, very few eosinophilic leucocytes, no mastzellen, and a megaloblastic crisis. The eosinophile cells during typhoid fever are usually very much reduced, and the failure of an increase when there is a high leucocytosis may be of value to those interested in these cells. There was no period of hypothermia while in the hospital, but the hæmorrhages had begun seven days before admission, and the temperature was not taken during that time.

Whether in this case, also, there was a severe local infection of the bone marrow as in Case I, cannot, unfortunately, be known.

These cases illustrate well the fact that very high leucocyte counts should be controlled by differential counts to avoid counting nucleated red corpuscles as leucocytes.

As we have mentioned above, such cases have been reported as examples of acute leukæmia, and in discussing acute leukæmia, features of such cases as these are sometimes given. (This question is discussed and references given in an article referred to above.) But we believe that the high percentage of polymorphonuclear neutrophiles, the relatively low percentage of typical myelocytes, and the very low percentage of eosinophiles, in connection with many nucleated reds, may allow us to keep these cases separated from the leukæmias. We know the cause of a few at least of these cases, while of true leukæmia the cause is still utterly unknown.

It is in the hope of stimulating a little interest in this problem, and because we judge that such a blood picture in typhoid fever is very rare, that the above cases are reported.

MRS. PACKARD AND HER INFLUENCE UPON LAWS FOR THE COMMITMENT OF THE INSANE.[1]

By W. R. Dunton, Jr., M. D.,

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In June, 1906, there came into my possession two volumes, the first entitled "Modern Persecution, or Insane Asylums Unveiled," and the second, "Modern Persecution, or Married Women's Liabilities, as demonstrated by the report of the Investigating Committee of the Legislature of Illinois," by Mrs. E. P. W. Packard, published by the authoress, and printed in Hartford in 1874. These books are bound in cloth stamped to imitate leather, with considerable gilding. The edges are gilt and the make-up of the books is not in keeping with their character. A glance at them shows that they were written by one of that class of chronic insane, who on account of the apparent mildness of their alienation are frequently enabled to cause great trouble to those who are responsible for them, and who oftentimes have been able to publish their experiences and to write them in such a way that they do not impress a person untrained in observing the insane as being abnormal.[2]

Mrs. Packard, I learned, had done so much that a closer study of her works and of the records of the times in which she lived has proved very interesting. Among other things, she is responsible for changing the laws regarding the commitment of the insane in Illinois and in Massachusetts, and I felt that possibly others might be interested in learning something about her.

A brief history is necessary for a proper understanding of her case. According to her own account, her maiden name was Elizabeth Parsons Ware, and she was born December 28, 1816, at Ware, Hampshire County, Mass. She was the only daughter of an orthodox clergyman of the Congregational denomination, and was married May 21, 1839, to the Rev Theophilus Packard, fourteen years her senior, who was a Congregational clergyman preaching in a Presbyterian church in Manteno, Kankakee County, Ill., at the time when what she terms her "legal prosecution" began. She had then been married twenty-one years, and she had borne six children, the oldest eighteen years of age and the youngest eighteen months. She states that she had been educated a strict Calvinist and her reasoning faculties had been developed through scientific education, so that by the simple exercising of her own reason and common sense she had been led to endorse theological views in conflict with her educated belief and with the creed of the church with which she was connected. Knowing that she had some original ideas in regard to religious belief she was invited by a deacon to join his bible class and present her views, with the idea of awakening interest in the study of the bible. The matter was referred to Mr. Packard, who acquiesced, and the patient accordingly presented a paper dealing with the free discussion of religious belief, rights of private judgment, etc., all of which were somewhat at variance with the Calvinist doctrine.

The discussion which was started led to an increase in the size of the class from six to forty-six, but it was felt by the orthodox deacons that Mrs. Packard's views were iconoclastic and that she should not be allowed to promulgate them, and in the following extract we find reference to the first effort made by her husband to stop these discussions.

"One afternoon Deacon Smith visited him [Mr. Packard] in his study, and held a secret interview with him of two hours length, when he left him a different man. That evening, just before retiring to rest, he remarked in a very pleasant tone:

"Wife, I want to talk with you a little while, come here." I went into his extended arms, and sat upon his lap, and encircled his neck with my arm, when he remarked in a very mild tone of voice:

"Now, wife, hadn't you better give up these bible-class discussions? Deacon Smith thinks you had better, and so do some others, and I think you had better too."

"Husband, I should be very glad to get rid of the responsibility if I can do so honorably, but I do not like to yield a natural right to the dictation of bigotry and intolerance, as Deacon Smith demands; but I am willing to say to the class that as Deacon Smith, and Mr. Packard, and others, have expressed a wish that I withdraw my discussions from the class, I do so, at their request, not from my desire to shrink from investigation on my part, but for the sake of peace, as they view it."

"No, wife, that won't do; you must resign yourself."

"Won't that be resigning, and that too on a truthful basis?"

"No, you must tell them it is your choice to give them up."

"But, dear, it is not my choice."

"But you can make it so, under the circumstances."

"Yes, I can make it so, by stating the truth; but I can't by telling a lie."

"Well, you must do it!"

"O husband! how can you yield to such an evil influence? Only think! Here you have pledged before God and man that you will be my protector, until death part us, and now you are tempted to become my persecutor! Do be a man,

[1] Read at a meeting of The Johns Hopkins Hospital Historical Club, March 11, 1907.

[2] Comparatively recently (1904) there was published in Baltimore a book of like character entitled "Sane or Insane? or How I Regained Liberty," by Margaret Starr, this being the pen name of Miss Stella Lawson, whose case occupied the papers for a brief period. It shows a great many similarities to the books under discussion.

and go to the class, in defiance of Deacon Smith, and say to the class: 'My wife has just as good a right to her opinions as you have to yours, and I shall protect her in that right. You need not believe her opinions unless you choose; but she has a right to defend her honest opinions as well as yourselves. I shall not suffer her to be molested in this right.'"

"Then you will be a man—a protector of your wife—and you will deserve honor, and you will have it. But if you become my persecutor and go against me, as Deacon Smith desires, you will deserve dishonor, and you will surely get it. Don't fall into this fatal snare, which the evil one has surely laid for you."

"He construed my earnestness into anger, and thrust me from him, determining to risk this result at all hazards."

"From that fatal time, all good influences seemed to have forsaken him, and he left to pursue a downward way, with no power to resist evil or flee from the tempter. Reason, conscience, judgment, prudence, consistency, and affection, all, all, directly sunk into the fatal sleep of stupidity or death."

"From that point, I have never had a protector in my husband. He has only been my persecutor! In a few weeks from that time, he forcibly entombed me within the massive walls of Jacksonville Asylum prison, to rise no more, if he could prevent it. He told me he did this, to give the impression that I was insane, so that my opinions need not be believed, for, said he, 'I must protect the cause of Christ!'"

Upon Mrs. Packard's refusal to discontinue her "missionary work" her husband wished her to visit her brother for three months, and take two of the children, but refused to allow her to have any money at all, although apparently she had a certain amount in her own right, and at the end of the discussion he threatened to send her to an asylum. She consulted a neighbor, who told her that it would be impossible for her to be incarcerated in an asylum without a jury trial, and that no jury would pronounce her insane. She then details how her children were alienated from her, how people were introduced into her house to spy upon her, how her things were taken from her and finally, how, on June 18, 1860, she was abducted, as she expresses it, and sent to the State asylum at Jacksonville. She states that the only medical examination that she had was when the two physicians came to her room and each felt her pulse without asking her a question or saying a word to her, and that she was incarcerated on a statute of the State of Illinois, passed February 15, 1851, which is as follows:

"Married women and infants, who, in the judgment of the medical superintendent (meaning the superintendent of the Illinois State Hospital for the Insane) are evidently insane or distracted, may be entered or detained in the hospital on the request of the husband of the woman or the guardian of the infant, *without* the evidence of insanity required in other cases."

It can readily be seen how such a statute as this was capable of causing much persecution. On Mrs. Packard's refusal to do anything which could be construed as a voluntary effort on her part to enter the asylum, she was picked up and carried to the train, and from the train to the asylum, where she was received by the assistant superintendent and was conducted to her "lone and solitary cell." The next morning she had quite a long conversation with the superintendent, Dr. McFarland, upon whom she apparently made a favorable impression, and a few days afterwards took leave of her husband, bidding him "good-bye forever."

She apparently got along well for the first four months of her stay at the asylum, and felt that Dr. McFarland was an honorable man. She states, however, that on one occasion he kissed her upon her forehead, and upon her reproving him he stated that it was only a kiss of charity. She was allowed free use of writing materials, and feeling that she had influence over Dr. McFarland she felt that she could induce him to treat the patients in a more humane manner than he did, and with this idea in view she wrote him a reproof, covering eighteen printed pages, in which she made certain threats after beginning in a most religious way. She was then sent to a "disturbed" ward where she remained for two years and eight months, and her accounts of what she did are extremely interesting.

It is difficult to judge the true state of affairs from Mrs. Packard's statements. At times she speaks of the filthy condition of the wards, the neglected condition of the patients, and of the cruelties to which they were subjected, and in another place will state how through slight efforts on her part or through a humane nurse everything was made bright, clean, and cheerful. This inconsistency in statement is a rather prominent feature throughout the book, which is put together in a most slipshod manner. Apparently each chapter was written as a separate essay, and there is consequently a great lack of consecutiveness. The patient wrote a great deal although she was supposed to be deprived of writing materials, but obtained them by various subterfuges, and it is difficult to reconcile her statement that she is a Christian woman with many of the underhand acts of which she was guilty. She was apparently meddlesome, and I imagine must have led the attendants and physicians a rather uncomfortable existence.

She intersperses her narrative with frequent histories of other patients and with condemnation or approbation of various attendants.

In 1861 she made an effort to interest the chaplain in her behalf, created a disturbance, and was carried back to the ward after chapel by a porter. It may perhaps illustrate Mrs. Packard's point of view to state that she met a patient at a ball, and on asking him his name was told that it was Jesus Christ, but that he was not the Jesus Christ who came to earth and was crucified, but another, and that in God's family all his sons were Jesus Christ as much as the first, as soon as they became perfectly developed in his spirit which the patient felt was perfectly developed in himself. In other words the patient felt that he was a perfect man in the estimation of Jesus Christ. Mrs. Packard asks, "Now, where is his insanity? Even his hobby, where has that gone?"

In September, 1862, a few days prior to the meeting of the trustees, she asked the superintendent's permission to read to them a paper directed at Calvinism. Mr. Packard was present on this occasion, and for fifty minutes the patient read "An Exposure of Calvinism and Defense of Christianity," the reading of which created such a good impression that she asked permission to read another document which was entitled "Conspiracy," and was an exposure of Dr. McFarland's and Mr. Packard's actions against her personal liberty.

Following this she was questioned by the Trustees, and she states that "The playful easy style and manner in which I made my statements seemed to dissipate the sentimental gravity of this august body so that they came to seemingly regard me as one of their number instead of a culprit under the grace of court! They manifested a willingness to do anything whatever that I asked." Mrs. Packard called their attention to the fact that her husband was not compelled by law to support her, that she had no legal protection of her person nor of her rights except through the voluntary act of her husband. The next day Dr. McFarland requested that she give him the documents which she had read, and promised that both would be printed. She wished to make certain changes, and ended by writing a book which was called "The Great Drama," of which she states:

"If, during my life-time, this 'Great Drama' can be published and not imperil my personal liberty, I shall be happy to give it to the world."

"But until that time arrives, when an original thought can be spoken or written, without incurring the charge of insanity for such an act, my personal liberty is only safe, while this manuscript is hidden from the age in which it was written."

The paper which she read on Calvinism forms Chapter LIV of her book. Following this occurrence she was treated very well, but after again threatening the superintendent she was again sent to a "disturbed" ward. The superintendent agreed to discharge her, but the trustees decided that she should only be discharged into the custody of her husband. This Mrs. Packard resented, and thereupon she was removed by force from the asylum just as she had been placed there June 18, 1863. This ends the first volume.

In the second volume Mrs. Packard states that she protested against again being placed in the hands of her husband because she knew that he would send her to an asylum in Massachusetts, but despite her protest she was put "into the absolute power of my persecutor against my will." Her husband placed her in the care of her adopted sister in Putnam County, Ill., with instructions that Mrs. Packard should never be allowed to leave, that if she did he would place her in another asylum. She made friends who agreed to stand by her in case of any trouble, and advised her to go to her children, and gave her the necessary money. She arrived at Manteno, her home, and happened to meet her little boy at the station. From him she learned of certain commands that Mr. Packard had made in order to prevent intercourse between her and her children. She was told by her husband that she was not wanted, and that she should not take any part in the household work nor interfere with the children in any way, but despite this, Mrs. Packard went about her household occupations and states that she had made up her mind never to speak in self-defense.

When she found the keys which were used to keep her from the household stores she appropriated them, and following this an active search was made of all her things and even the house, she finally being locked up in a room so that she could have no opportunity of using these keys. The windows of her room were nailed down and her meals were brought to her. She was not allowed to communicate with anyone excepting her own family, but for six weeks she taught her four children arithmetic, grammar, etc., she having at one time been a teacher.

Mr. Packard accidentally left a package of letters in her room from which she learned that in a few days she was to be entered into the "Northampton, Mass., Insane Asylum, for life." She comments upon the fact that the superintendent, Dr. Prince, was willing to receive her as a case of hopeless insanity on a certificate of Dr. McFarland without any sort of a trial, and that Mr. Packard's sister had evidently assisted him in making the arrangements for her transfer.

She also learned that the trustees at Jacksonville were willing to receive her again as a patient. She was able, shortly after, to send a note to her friend, Mrs. Haslet, by means of a passer-by, and a writ of habeas corpus was secured. Mrs. Packard then had a jury trial which continued five days. She reports this trial, which took place in January, 1864, at considerable length, by means of statements of various persons concerned in it. The only ground upon which this trial was secured was the fact that she was kept a prisoner in her house.

Following the trial she found that Mr. Packard had removed in the meantime to Massachusetts, and she had been deprived of her property and was without means of support. In attempting to gain possession of belongings which had been left in the charge of her brother-in-law she committed certain acts which were said to have been illegal and in which the question of her nonentity, because she was a married woman, was brought out somewhat prominently.

In order to support herself Mrs. Packard decided that she would publish her book entitled "The Great Drama, or the Millennial Harbinger," and sold tickets at fifty cents each, by means of which she raised $700.00 and was enabled to have 1000 of these books printed. After she had sold about 6000 books she visited her father in Massachusetts, was forbidden by Mr. Packard to see her children, but succeeded in winning her father to her cause, and he became her protector. She thought it necessary to "seek the protection of the legislature of Massachusetts by petitioning them for a change in their laws on the mode of commitment into insane asylums." She introduced two bills into the Massachusetts legislature, one that "No person shall be regarded or treated as an insane

person, or a monomaniac, simply for the expression of opinions, no matter how absurd these opinions may appear to others," and the other that "No person shall be imprisoned and treated as an insane person except for irregularities of conduct, such as indicate that the individual is so lost to reason as to render him an unaccountable moral agent."

She also succeeded in having the mode of commitment changed so that instead of allowing the husband to enter his wife at his simple request, added to the certificates of two physicians, a form of commitment now in force in Maryland, it was necessary that the husband get ten of the wife's nearest relatives to join in the request for admission to an asylum, and made it possible for the patient to communicate with any of these ten relatives beside two other persons who might be designated. With the passage of this law Mrs. Packard felt somewhat secure.[3]

Mrs. Packard interrupts her narrative here to villify her husband and to explain why she did not get a divorce. As has been stated before, her narrative is not consecutive, and of itself indicates mental instability. She also narrates a dream which she had had while at Jacksonville, and in the interpretation of which she had been assisted by a woman in charge of the sewing-room. She also speaks of having been warned two and a half years before her admission to Jacksonville by spiritualistic communications, of her impending troubles. She speaks of Mr. Packard's monomania and says that three years before his plot culminated that she had visited a lawyer in New York State to obtain advice on the subject of woman's rights, from which it may be inferred that Mrs. Packard had been active in other propaganda than bible teaching. She states that Mr. Packard was examined by Mr. Fowler, the great phrenologist, who expressed his opinion somewhat as follows:

"Mr. Packard, you are losing your mind—your faculties are all dwindling—your mind is fast running out—in a few years you will not even know your own name, unless your tread-mill habits are broken up. Your mind now is only working like an old worn out horse in a tread-mill."

After preparing the ground by obtaining testimonials and making friends, Mrs. Packard left Massachusetts in the winter of 1866 and came to Chicago to organize an effort for the passage of the Personal Liberty Bill of married women. She brought the matter before the governor, whom she enlisted upon her side, and after considerable work on her part, opposed as she believed by opposition organized by Dr. McFarland, she succeeded in having the bill passed.[4] This bill provided that no person should be incarcerated in an asylum for the insane without a jury trial; and that all patients then in such hospitals should be given a jury trial. This bill was approved by the governor March 5, 1867. An investigating committee was also appointed, who reported adversely upon the asylum management and recommended that Dr. McFarland be removed. Mrs. Packard interpellates considerable testimony from attendants and former employees, etc., all derogatory to the hospital management, and gives an account of how Dr. McFarland had "cruelly punished a perfectly sane patient" for striking an attendant, and also how he had made an improper proposal to a sister of one of the patients.

The Board of Trustees, who alone had authority to remove Dr. McFarland, was appointed by the governor, and in order to shield themselves requested that they be re-appointed, agreeing to discharge Dr. McFarland. This they did not do, but re-appointed Dr. McFarland and resigned themselves, thus keeping Dr. McFarland in office for a further period, as no further steps could be taken tending toward his discharge until the next session of the legislature. Dr. McFarland resigned before this met, and in this manner was cleared from any opprobrium which might attach itself to him.

Mrs. Packard next turned her attention to Connecticut, and made an attempt to have the laws for the insane changed in that State, but was not successful.

During the session of the Iowa legislature of 1872 she made a great effort to have a bill protecting the rights of the insane passed and was successful.

The remainder of the book is made up of arguments concerning her past work, narratives of ill-treatment of patients at Bloomingdale, Trenton, and other hospitals, and a number of statements as to her own employment, from which we learn that she settled down in Chicago with her children until they gradually left her to seek new fields of occupation.

From Mrs. Packard's own statement, as contained in these volumes, we have learned that she was instrumental in changing the commitment laws of two States, Massachusetts and Illinois, of securing the passage of a bill to protect the inmates of insane asylums of Iowa, and secure the patient's right of free correspondence, and also of having the superintendent of the Jacksonville Asylum removed from office.

From these same books we also formed the opinion that Mrs. Packard was a chronic lunatic whose judgment was impaired, and who in all probability might be controlled by delusions, and the question of diagnosis is an interesting one although it is impossible to be strictly accurate. She evidently belonged in a rather large group of cases whom Magnan placed under his *délire chronique,* and by others grouped as chronic delusional insanity, in which the symptoms are not especially well defined. Her condition also may be classed either as a menopausal or a conjugal psychosis. At the time of her incarceration in Jacksonville she was 44 years old, about the time when her climacteric might be supposed to have begun and after she had accomplished certain reforms she seems to have settled down to a quiet life, possibly at the expiration of her climacteric and the subsidence of the mental symptoms. The fact that her husband was 14

[3] These bills were presented to Committee of Lunacy, March 29, 1865, and form Chapter 268, Section 2, "Laws of Massachusetts."

[4] In the American Journal of Insanity, Vol. 22, page 548, in a review of the report of the Jacksonville Asylum, for 1864, Dr. McFarland speaks of mild cases of insanity and of the trouble that they may cause, but makes no specific reference to Mrs. Packard.

years her senior may have been an added factor, and while there seems to have been no open rupture between them, preceding his declaring her insane, there may have been some waning of their affection. It has been difficult to find any literature upon the other side of the case, but the following was obtained after a good deal of trouble.

On May 19, 1863, Dr. Andrew McFarland, at the meeting of the American Association of Superintendents of American Institutions for the Insane, held in New York City, read a paper entitled "Minor Mental Maladies," which is printed in the Journal of Insanity, Vol. 20, Page 10, July, 1863, and in the discussion which followed the reading he relates (page 89) a case history, which is evidently that of Mrs. Packard. According to this she was admitted to Worcester Hospital when 20 years of age; her father was a man of sufficient wealth to have given her a superior education, and she was very accomplished; she possessed a fine personal appearance, and was a model of a young lady in respect to her moral, physical, and intellectual qualities. At 19 years of age she was the principal teacher of a first-class Massachusetts female school. Her mother had been insane for many years. About five or six years after her marriage she began to thwart her husband in little matters, but he kept the facts to himself, but matters becoming too troublesome he removed to the State of New York. The same disposition again showed itself and he again removed, going to Ohio, and about 1857-58 they came to Illinois. Dr. McFarland could not, at the time of her admission, discover any intellectual impairment at all, but states that "her hatred of her husband had something diabolical about it; every instinct of love was banished from her. She was thoroughly demoralized and corrupted in all her moral sentiments. . . . She informed me that her husband was the great 'red dragon' and that her eldest son was the 'man-child' mentioned in the same Apocalyptic connection, and that was the only delusion discovered in two and a half years."

Dr. McFarland states that she gave him infinite trouble, and then speaks of her paper on Calvinism to which reference has been made above.

In writing her book "the whole delusion which had lain concealed in her case for eighteen years became fully developed, and it showed that all this perversity of conduct arose out of one single delusion; and the delusion was, that, in the Trinity, distinctions of sex had to exist; that there could be in the Trinity no more than in the family unity of sex; that there must be a distinction of sex, and that she was the Holy Ghost."

From his remarks Dr. McFarland evidently believed the case to be one of moral insanity.

In the *American Journal of Insanity*, Volume XXVI (Oct., 1869), page 204, there is a review of five pamphlets dealing with the Illinois legislation regarding hospitals for the insane which begins as follows:

"For the last two or three years, or more, the State of Illinois has been singularly under the influence and dictation of a handsome and talkative crazy woman, and of a legislature prompted by her to be crazy on at least one point—that of the State Hospital for the Insane—as if they expected some day to inhabit there, and wanted to make of it, in advance of their going, as lawless a place as a legislative hall in these days is commonly reputed to be."

This vein of sarcasm is carried through several pages, and attention is called to the fact that during Mrs. Packard's confinement in the State Hospital "the idea, not very irrational, that the kind and civil superintendent was, in her own phrase, a true man, made in the image of God, and whom she might adore in preference to any 'red dragon'" (her husband), her offer of attachment being unreciprocated, she turned upon Dr. McFarland. The above statement is in measure borne out in her own works.

Criticism is made of the manner in which the committee carried out their investigation of the hospital mismanagement. The fact that but few of the meetings were held at the hospital, that the meetings were not published, that no publication was made of evidence offered, and that the accused persons, excepting only the superintendent, were not given an opportunity of hearing the charges made against them and of making excuses, being the chief points of attack.

The question of the manner of taking evidence is discussed at some length, and also a statement is made of the position of the hospital toward the patient, it being claimed that it stands *in loco parentis*.

Quotation is made from the report of the Trustees as to their manner of carrying out the provisions of the Personal Liberty Bill, from which I quote the following:

"Three sets of cases seemed to grow out of this stage of the transaction:

(1) Those maintaining entire silence.

(2) Those refusing participation in any proceeding.

(3) Those desiring trial.

These latter had their subdivision into those requiring trial at the institution and those wishing it at their homes. The result of these inquiries (made in a manner to give the utmost freedom in reply) will throw some light, hitherto unperceived, on the feelings of the insane. The first class was most numerous of any; the second was next in point of numbers; and the third class least of all; and of those expressing inclination for trial, eleven, only, desired such trial to take place at their homes. On communicating the wish of the latter number to their legal representatives, the refusal was unanimous to be at the expense of such transportation."

Just criticism is made of this manner of committing a sick person to a hospital, and the contention is made that it would be as well to hold a like investigation of other sorts of hospitals.

An example of how detrimental a public jury trial may be for an insane person is given, and in conclusion this backward step by the State of Illinois is deplored.

From the *American Journal of Insanity*, Vol. XXVII (October, 1870), page 260, we learn that Dr. McFarland, the late Superintendent of the Illinois Hospital for Insane, has proposed himself as a candidate for the State legislature of

Illinois; with the hope, if elected, of enlightening the people of that State on their public charities. "A fascinating crazy woman, who managed to seduce partisan prejudice and ignorance for her allies," is referred to as well as the recent legislation, and quotation is made from Dr. McFarland's manifesto upon the subject.

In the same journal, Vol. XIX (October, 1872), page 251, Dr. Ranney, Superintendent of the Iowa Hospital for Insane, at Mt. Pleasant, refers to the recent bill and speaks of Mrs. Packard's agitation, saying that from information he had received, the "legislation had been brought about by the grossest misrepresentations of this person, Mrs. Packard."

In the same journal, Vol. XXX (October, 1873), page 175, in a report of the proceedings of the Association of Medical Superintendents for Asylums of the Insane, Dr. Gray, Superintendent of the Utica State Hospital, states that "There have been some attempts to modify legislation in our State. We have had Dr. McFarland's former patient, Mrs. Packard, in consultation with the legislature. She did not accomplish much, however, in the introduction of Illinois and Iowa Bills, or what she called the 'Personal Liberty Bills'; and further says: 'She had two or three bills there and might have done some mischief, but the fact was too apparent that she had herself a record, and that record is in the proceedings of this Association, in the discussion in New York, a good many years ago.' I was asked in regard to the matter, and replied by handing her case to a member of the committee who had this matter in charge, as given in the *Journal of Insanity*, by Dr. McFarland, some years ago. Also a report of the legislative investigation into the affairs of the State Asylum of Illinois; a part of which proceedings contained the matter of her claiming Dr. McFarland as her affinity, that the doctor was the first person who had fully sounded the depths of her connubial life, that she was the third person in the Trinity, and her son was Jesus Christ. One of the waggish members hearing this, naively remarked 'that he did not want to oppose her, because he would be resisting the Holy Ghost.' She conceives it to be her divine mission to visit all the States, and does not believe in her insanity. I suppose she will soon be up in Massachusetts, at least we commend her to some other State."

In the same journal, Vol. XXXI (October, 1874), page 138, we find the following: "In relation to the subject of legislation we have had a little experience with Mrs. Packard. She is still with us, button-holing legislators, and pressing her bill. After her appearance before the legislative committee on public charitable institutions, it was evident they were satisfied, that her statements were entitled to receive little attention, and also with the unsoundness of the views of those who appeared in her behalf. It is true, however, that this committee, probably from motives of policy, reported to the legislature that it would be expedient to increase to a limited extent, the authority of the Board of State Charities, and directed superintendents to allow patients to write, free from any supervision, to this Board."

The above remarks being made by Dr. Eastman, Superintendent of the Worcester Lunatic Hospital, Worcester, Massachusetts, and on page 151 of the same, Dr. Basset, Superintendent of the Iowa Hospital for Insane, at Mt. Pleasant, refers to the law permitting unrestricted correspondence as follows: "We have now had two years of such legislation, and excepting a few modifications, scarcely lessening the evil which has abundantly developed under the practical working of the law, it still stands upon our statutes, a monument of unwisdom."

He then states that the hospitals have been visited regularly by a visiting committee to whom complaint has been made and who have investigated the same, and says that the above law was changed last winter so as to lessen the amount of letter-writing, so that the patients are now permitted to write under seal only to the visiting committee and only receive letters addressed to them from the committee without inspection, and says: "I have desired to call your attention thus briefly to this matter, for the reason partly that Mrs. Packard, the author of our law, is not idle, and I have reason to know intends to prosecute her efforts in other States. I heard her declare it to be her intention to make this her life work."

I have been unable to learn when Dr. McFarland resigned, but he subsequently established in Jacksonville a private hospital called Oak Lawn. Apparently he was well thought of by his associates. Neither have I been able to learn what finally became of Mrs. Packard, but I hope that later I may be able to settle these points.

NOTE.—Since the above was read it was learned that Dr. McFarland died at Jacksonville, November 22, 1891. It is understood that Mrs. Packard survived him. One of her sons was associated with Dowie, but after a quarrel with the prophet left the organization. Several of his children have been treated for nervous disturbances.

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ON THE IMPORTANCE OF SIMPLE PHYSICAL AND PSYCHICAL METHODS OF TREATMENT.[1]

By William Sydney Thayer, M. D.,

Professor of Clinical Medicine, Johns Hopkins University, Baltimore.

In accepting the kind invitation of your president to speak before you this evening, it has occurred to me that it may not be out of place to express a few thoughts with regard to the importance of certain simpler physical and psychical methods of treatment of disease. That which I am about to say may seem trite to many in this audience, and yet, although the conditions to which I am about to refer are tacitly recognized by many, nevertheless, as a profession, we have been rather slow to meet them as we should. We must all agree that the end of the efforts and studies of the physician should be to prevent or heal or ameliorate disease—to further and perfect the *art of medicine*. And while recognizing our inefficiency and helplessness in many respects, we must realize what enormous advances have been made in recent years. If one looks back, however, at the history of medicine during the last century he cannot fail to be impressed with the fact that the first nine decades of the nineteenth century, associated as they were, with progress in the medical sciences, such as has rarely been recorded in a like period of time, were yet not to a like degree fruitful in advance in the *art of practice*.

Based on the anatomical foundations laid by Morgagni and Bichat and extended by such men as Müller, Schültze, and Virchow, a brilliant line of students, Auenbrugger, Laënnec, Corvisart, Skoda, and others introduced accurate methods of detecting changes in organs and tissues *intra vitam*. At the same time their associates and followers, Bright, Addison, Bouillaud, Schönlein, Louis, and Trousseau, not to speak of their numerous living students and successors, by careful and acute clinical studies, laboriously correlated with the anatomical appearances at autopsy, developed a degree of diagnostic exactitude which transformed medicine. And this period of anatomical study was associated with and followed by the great awakening in physiology and experimental medicine started by Magendie and continued by Claude Bernard, and later by the brilliant bacteriological and parasitological studies initiated by Pasteur and Koch, and by that progress in physiological chemistry which is throwing day by day more light upon the functions of the human body in health and disease.

But throughout the greater part of the last century the minds of the bulk of active scientific investigators were occupied with the anatomical, physiological, and bacteriological study of disease, and the clinical application of their methods and results to *diagnosis*. At the same time a realization of the folly of the old, blind expectations as to the specific action of many drugs and the possibility of influencing regressive structural changes by medicine, brought about, it must be acknowledged, a certain therapeutic pessimism. The medical world became more and more interested in *sedibus et*

[1] Delivered before the Louisiana State Medical Society at New Orleans, May 14, 1907, and appearing in the N. O. Med. & Surg. Journal.

causis morborum in which discoveries were daily made, than in attempts to detect new methods of treatment. Some of our medical clinics became, as has been said, great diagnostic institutes.

While among the wiser members of the profession this interest in pathological anatomy and bacteriology and chemistry, in the scientific study of disease, and the realization of the folly and vanity of random experiment on the human being with new drugs with the expectation of finding new medicines with specific action against disease, brought about only a judicious conservatism in practice, yet, in other less balanced minds, an overpowering interest in one side of the question led to a lack of that attention to the details of the art of healing which, after all, is the final duty of the physician to his patient.

But it cannot be said that the condition of the patient suffered. In those very clinics which were most criticised and most vehemently accused of therapeutic nihilism the treatment of the patient was steadily improving. The delivery from poly-pharmacy, the employment of the simpler physical means of treatment, instead of constant, aimless experiment with drugs, with the action of which we were wholly unfamiliar, and which more often than not were harmful rather than beneficial—these were great blessings. But the tree of medical science had not yet begun to bear its first fruit of real improvements in the art of healing. In the last twenty years, however, great changes have come to pass. The introduction of scientific methods of study into certain branches of medicine have inevitably brought about habits of more exact thinking in other branches. Let us consider for a moment some of the changes which have been taking place in the practice of medicine as a result of the development of more scientific methods.

(1) As I have already said, men trained in exact methods of thought and action could not fail to realize the folly and danger of an indiscriminate use of drugs. Several years ago, while reading, on a railway train, a book lent me by a distinguished teacher and master, whose name many of you may guess, I found on a slip of paper between the leaves, the sketch of a thought upon this very question which expressed well that which we should feel. What surprising and unlooked-for reactions might occur if we were to drop chemicals at random into a glass found standing in a laboratory and containing a fluid of unknown constitution! We might well hesitate to risk the experiment. And yet, as physicians, we have been in the habit of introducing thoughtlessly into the complex chemical fluids of the body, an infinite variety of substances with the nature of which we are too often unfamiliar, without the least conception of what far-reaching evil effects our act might have. This may seem an exaggerated statement. But let me take one example. Nearly twenty years ago, a new antipyretic, highly recommended—as they always are—was placed in the hands of the profession. This was used on a number of patients in the wards of a large hospital. Ill effects were soon noticed. Experiments were made upon animals and the drug was found to be one of the most powerful destroyers of the blood with which we are familiar. Only a few months ago it was chosen by one of my colleagues as the best type of poison to administer to animals for the purpose of producing experimental anæmia, in order to study the regenerative changes in the bone marrow. Its constitution was not unlike that of other antipyretics which are relatively harmless in their effect, and to its thoughtless use in different parts of the world we cannot doubt that many human lives were sacrificed. The harm which may be done by the pointless and careless use of drugs often outweighs any possible advantages. We are coming to realize that as far as possible we should use only drugs, the physiological action of which we understand, and which can be easily controlled. We must, as physicians, know what we are doing and consider carefully before entering on medical experiments. And experimental physiology and pharmacology are reproducing and solving for us many a problem which, in the human being, would be difficult or impossible to approach.

(2) One of the first and most brilliant advances in therapy dependent upon careful physiological study and observation was the introduction by George Murray of thyroid feeding in the treatment of myxœdema and cretinism. It is true that no similar animal extract has as yet proved of like efficacy, but the discovery has opened a hopeful field for future study and the recent observations of MacCallum concerning the use of the extract of parathyroid glands in tetany, may prove of almost equal importance.

(3) Consider again the immense progress associated with the development of the use of the antitoxine of diphtheria, and to a lesser extent, that of tetanus; with the hopeful action of preventive vaccines against typhoid fever, cholera, dysentery, and plague, and the studies upon opsonic immunity—the opening of the whole field of specific serum prophylaxis and therapy.

One must, with regret, pass with a mere word of reference the wonderful results of preventive medicine in yellow fever, malaria, plague, and cholera, which have been achieved through systematic scientific study of the nature of these diseases, their mode of transmission, and the conditions under which they prevail.

(4) The fascinating investigations of Ehrlich and his students as to the manner of action of various chemical substances in different infections give us ground for hope that ere long principles and laws may be discovered, the therapeutic value of which we cannot to-day estimate. Everywhere there are signs of re-awakening of therapeutic enthusiasm—an enthusiasm based on the fact that the seeds which science has so patiently and sedulously sown are germinating and bringing forth a new therapeutic art, born of research and experiment, accurate thinking and reason—widely different from the blind empiricism of the past.

(5) Almost equally important, though not perhaps as brilliant as these more specific measures, is the awakening which is gradually coming over the profession with regard to the enormous therapeutic reservoir which we have in the rational and carefully planned application of the more simple physical

and mental methods of treatment. Few of us often consider the part that the pure physical and psychical methods of treatment play in the care of the great majority of maladies which come under our observation. It is no exaggeration to say that these methods are the most important that we have. The difference between modern therapy, or, we must probably say, the therapy of the near future, and that of the past, is going to be, it seems to me, largely the difference between using these methods blindly and without a realization of what we are doing on the one hand, and on the other, of applying them intelligently and with a full conception of the opportunities which lie before us. As it is, we are only beginning. We often forget and neglect.

Let us take a few examples and consider that which we do and that which we might accomplish.

If one of us be tired and worn out from loss of sleep, what do we do? Is our first act to take a tonic? No. It is, if we can, to rest and sleep.

If, from overwork and strain, we find ourselves nervous and perhaps sleepless, what do we seek to do? To take a hypnotic? No. If possible, we take a vacation. And we know that if we can get away from the hurry and cares of daily duties we shall recover immediately. The tonic and the hypnotic are makeshifts—and sometimes dangerous makeshifts.

If there come to us a woman who, in the same way, from constant strain and care, added, it may be, to an inherent instability of body or mind, has become worn out, introspective, and neurotic, do we not to-day realize that in the majority of cases that which will best start her on the right path is to separate her from her surroundings, to put her to bed, to give her a trained nurse who shall have had experience in caring for individuals in like nervous or mental conditions; to carefully re-educate, as the popular term now is, the digestive functions, by beginning with the simplest and most limited nourishment, gradually progressing until the patient, without realizing the fact, is taking a full diet; by the induction of medical obedience; by constant and carefully planned mental encouragement and stimulation, and later, by exciting the patient's interest in some bodily or mental occupation, to take her mind from herself, while at the same time, by the use of massage, baths, packs, and perhaps electrical treatment, the skin is kept in good condition and the muscles in such a degree of nutrition that, when she again seeks to use them, she may find herself reconstituted in body as well as in mind? This is what the Weir Mitchell rest cure, lately so ably set forth by Dubois, means. When, after two or three months, the patients, as they often do, return better and stronger than they have been for years, we hardly realize that the treatment which they have received has been purely physical and psychical, that those medicines which have been employed, if indeed, any have been employed, have played a wholly secondary part.

Again, let us consider the conditions in typhoid fever. We have for some time realized well enough that it is useless to attempt to treat locally and by internal medication that which long before the time it is recognized, has been a general septicæmia. To expect to cure typhoid fever by disinfecting the intestinal tract, even if it could be done, would be just as absurd as expecting to cure a case of secondary syphilis by local treatment of the cutaneous manifestations. What do we do? The first thing on which we insist in the treatment of a case of typhoid fever is physical rest, that the heart and muscles which are already weakened by the circulating toxic substances may not be overstrained. We regulate the diet so that the patient may be supported as far as may be, that the loss of body nitrogen may be kept at the lowest possible point, while yet avoiding such nourishment as may in any way interfere with the somewhat impaired digestive processes. We use cold water in the form of baths or spongings or packs for its remarkably stimulating effect on the general mental and nervous condition of the patient, and for the apparent benefit which results from the coincident lowering of the temperature. But what we often forget is that such baths and spongings should always be associated with careful massage. It is one of the commonest defects in our treatment of typhoid fever, and other prolonged maladies, febrile and afebrile, that we forget to look out for the condition of the muscles. We should never think of putting a neurasthenic upon a prolonged rest cure without insisting upon massage and hydro-therapy in its various forms in order to prevent the atrophy which follows long disuse; but in these other conditions in which, as in typhoid fever, there is greater muscular degeneration as a result of the toxæmia, we too often entirely forget the great importance of massage, and abandon it, if it have been given, with the falling temperature and the discontinuance of the baths. Every typhoid fever patient, after his temperature has fallen, should still have at least one alcohol sponging associated with thorough general massage daily. It is surprising to see the difference in the strength of a patient with pneumonia, for instance, who is given general massage as soon as his temperature falls to normal, and that of the man who passes his convalescence entirely at rest. The one finds his legs strong and ready to bear him; the other, with a heart weakened by disease, finds his muscles far less able than they were before to support him; extra effort is required, more strain is put upon the heart, and the process of learning to walk again is a far more serious matter. There is, it seems to me, really greater need for proper attention to the muscles in typhoid fever and in convalescence from pneumonia than in the treatment of a neurasthenic.

The same applies to the treatment of patients with all manner of surgical injuries. The difference between the condition of him whose muscles have been carefully attended to and that of his fellow who arises with a general atrophy of disuse is enormous and can be appreciated only by one who has seen the two conditions.

Consider for a moment the treatment of diseases of the heart, muscular or valvular. Rest and regulation of the manner of life of the patient are here the essential features—medicines should be the last resort. There are conditions of lack of compensation in which rest alone is of course insufficient, where the brilliant effects of digitalis, diuretics, and

purgatives are happily familiar. But excepting at such a period, the problem in the great bulk of conditions associated with weakened heart, is another. It is a question of bringing the heart back into training. The task before the patient with a dilated heart differs from that which is to be met by the young man who is training for a race only in degree. On the one hand, it is a question of taking steps to prepare normal muscles and a normal heart to withstand extraordinary effort. On the other, 'tis to prepare a weakened heart to bear burdens which, for a healthy man, would be normal. The brilliant results so often obtained at Nauheim and elsewhere by the application of those measures elaborated by Schott and others, which consist simply in lessening the burdens of the heart through the baths and by gradualllly training it to increased effort by means of carefully graduated and progressively increased resistance movements, show how much can be accomplished by the simplest physical measures when carried out in an exact and painstaking manner, according to a carefully laid and scientifically controlled plan of action. Only with loss of compensation—that loss of compensation which may be so long delayed by purely physical methods of treatment—do we fall back upon digitalis to save the day. And at the very end, when digitalis has failed, it is the lancet which gives the patient a new lease of life.

Let us consider again the treatment of a colitis, say an amœbic dysentery. The first necessity is absolute physical rest; next, regulation of the diet, and lastly, the question of medicine. And medicine by the mouth, as we so well know, is of little value here. In the end it comes to the use of irrigation of the colon with water judiciously medicated.

Similar considerations apply to the treatment of pulmonary tuberculosis. In no disease have so many drugs been employed; in no disease have so many fantastic methods of treatment been advised; in no disease are the essentials so well met by the careful carrying out of simple physical and psychical methods. Absolute rest, especially if there be fever. Freedom from care and responsibility. Careful attention to the diet. Life in the open. Above all, the placing of the patient in a position in which, from a mental standpoint, he may be encouraged and stimulated. In no disease is attention to the environment of the patient—the importance of which has been so ably emphasized by James—more necessary than in pulmonary tuberculosis. Year after year hosts of poor consumptives go forth in search of that far-off climate which, alone and unaided, is to bring them back to health. As well might they seek the fountain of youth! Allured by the enchantment of distance, they abandon the comforts of home, the restraining influence of wise advisers, the encouragement of companionship and example, for a cheap boarding-house or the solitude of the plains, and strangers in a strange land, homesick and doubting, writing thousands of miles for the advice which should be near at hand, they die in the midst of that paradise of which they had dreamed for the want of the hundred little physical attentions and mental stimuli which are the most important elements in the care of the tuberculous patient. The psychical stimulation associated with treatment in sanitaria is not the smallest element in its success.

One might go on through the whole list of human ills, not excluding those for which we happily possess drugs with specific effect. Indeed it may be worth while to refer briefly to the necessity of attention to the simple physical and mental side of the treatment of disease such as syphilis and malaria, types of the latter maladies. I think of a specific instance—a colleague who consulted me some years ago, with grave involvement of the central nervous system following accidental luetic infection in the practice of his profession. Despite vigorous treatment he had grown progressively worse. The outlook seemed almost hopeless. But it was noted that he had attempted to combine the treatment with attention to his daily duties. It was insisted that he leave home, take to his bed and put himself under the absolute control of a wise physician and nurse. Six months later a robust, healthy looking man entered my consulting room—I had not known him. The medication had not varied essentially from that which he had given himself, but the physical rest, the freedom from care and responsibility, the attention to his general bodily condition, and the mental encouragement and stimulation had turned the scale. 'Tis a common picture.

In like manner we are all familiar enough with the ease with which the milder forms of malaria may be treated, if the patient be willing to spend a few days away from work and at rest; how much less quinine will accomplish a good result, while the necessity of rest in the treatment of the severer forms of the disease needs no mention.

It is undoubtedly true that wiser physicians always have recognized and taken advantage of these facts. True success in practice is usually dependent upon the attention of the physician to the little physical and psychical details of his work. But the world at large takes a very different view of the practice of physic and it is ever amazing to see how deep-rooted is its faith in medical magic. Nevertheless, the public is slowly and half unconsciously beginning to appreciate these things. One of the most interesting evidences of this is in the rise and development of the trained nurse. What does the patient mean when he says, as he so often does, that, after all, a good nurse is more important than a physician? He means that the measures carried out by the trained nurse, the care she has taken of his skin, his muscles, the judicious preparation and administration of his diet, the little attentions which promote his general physical comfort, the confidence inspired by her cheerful and tactful behavior, have had more to do with his recovery than any other prescription that the doctor has given him—and he is right.

And what does our increasing dependence on the trained nurse mean? It means simply that we know that physical and psychical details of treatment are the most powerful measures which we can apply in our efforts to bring our patient back to health—that we have in the nurse an individual highly trained in the application of these measures.

What, indeed, is the secret of the success of that gentry who use their hands so much better than they use their heads, the

so-called Osteopaths? Is it not in great part that, by practice and experience, many have become fairly skilled masseurs whose treatment is of real value to the admiring patients whose "dislocated" vertebræ they so marvelously manipulate?

But why have I dwelt so long upon these rather simple points? Because it seems to me true that although many of us may realize where our power lies, we have been delivering over the application of these important methods of treatment to the trained nurse and to the surgeon, while standing aloof, in some instances with a traditional and pharisaical pride in the thought that we are not as the osteopath—we use our heads only—not our hands—an attitude which is a fatal stumbling-block to progress in the *art of medicine*.

Must we not, on reflection, be painfully conscious that not one of us has ever been properly instructed in massage, and that few of us are familiar with the many ways in which hot and cold water may be used to advantage? And if, indeed, one of us have worked in a part of the world where methods of physical therapy are properly taught, where is he to find the establishment in which his prescriptions can be suitably carried out?

The tired business man consults us in the summer. He cannot take a vacation; he has no horse. The country club where he might take the several afternoons a week of golf which would do him so much good, is too far away. A few hours a week of suitable hydro-therapy and massage and Swedish movements would give him an excellent substitute for the life and exercise in the open which is the medicine that he needs. But what have we, as a rule, at hand? Only the Turkish bath, which is often far too exhausting for a man in his condition, and the charlatan who poisons his mind and plunders his pocket.

In one city an interesting beginning has been made. A few years ago several members of the medical profession, recognizing the need of an institution for hydro-therapy, massage and other methods of physical treatment, succeeded in raising a moderate sum of money, as a result of which suitable rooms were obtained and fitted out with a satisfactory system of baths. A male and a female attendant were appointed, each trained in massage and Swedish movements. The establishment was put in charge of a young physician who was well qualified by study and experience. The institution is open in the morning for women, in the afternoon for men. The physician under whose general charge the establishment is placed—who, by the way, is an active man in all respects—a teacher and an investigator—has published a small pamphlet with a description of the various methods of hydro-therapy and the conditions under which they may be best applied. A patient may be sent with definite prescriptions for whatever treatment may be desired and this is faithfully carried out by the attendants. A moderate fixed fee is charged for each treatment. After two years the establishment became self-supporting and now it is making a good income, which might well, some day, be applied toward the establishment of a department for thorough instruction in methods of physical therapy in a neighboring university. I wish that I might say that this institution were in Baltimore.

In general, however, we are sadly behind our colleagues on the continent. In connection now with many of the better hospitals, there are properly organized institutes for physical therapy—institutes to which a patient may be sent for massage, for the various forms of hydro-therapy or for fitting exercises. I know of but one hospital in this country which has a thoroughly developed department of this sort. At the Massachusetts General Hospital, through the generosity of a lady in Boston, there is a complete set of Zander apparatus which has been of the very greatest assistance, while of late a system of baths has been added.

That upon which I would particularly insist is that we are neglecting a very important feature of medical education. We should give more time in our schools and hospitals to instruction in the *care of the patient* in its more literal sense. Courses should be given to the students in the essentials of nursing. The student, as well as the nurse, should be trained in massage, in Swedish movements, in hydro-therapy, in electro-therapy. Few physicians in active practice may have time to give massage personally. But many a young man could accomplish much were he able to give proper massage and to direct specifically suitable measures for the physical development of the tired, nervous patient, who now receives, if he be lucky, a little advice which he cannot carry out and a prescription for tincture of nux vomica, or, all too frequently, alas, a depleting diet and an elaborate course of medicinal treatment directed at his poor stomach, which, tired with the rest of his frame, has happened to attract his special attention and has been made the scapegoat.

If this be true with regard to the simpler physical methods of treatment, how true is it also in connection with the psychical influence which the physician should exert on his patient. As has been said above, true success in practice has always depended on the attention of the physician to the little physical and psychical details of his work. The encouragement, the stimulation, the mental lift which the good physician gives to his patient are the most important elements in his practice. This you may say is nothing new. No, indeed, it is probably as old as man, and as has been said, many thoughtful, conscientious physicians fully understand it. They realize that the good which they accomplish depends not so much upon the contents of their prescriptions, as on the time which they give to their patients, on the honesty and simplicity with which they explain to them the nature of their condition, and the earnestness with which they give of their own store of common sense and reason and optimism to the doubting and anxious invalid.

But do we always reflect that this power of suggestion, this mental control which the physician should exert over the patient is not universally comprehended? And is it not true that before our students we rarely insist upon such matters as clearly as we ought? We are rather accustomed to expect them to absorb these conceptions by intuition—and the results are sometimes odd. I think of an amusing example which

may serve as an excellent illustration. A young woman left a medical school at the end of her third year and became a Christian Scientist. When asked the cause of her action she is said to have replied that she had discovered that her professor of medicine—a most successful practitioner—was after all, nothing more than a faith healer, and that she therefore felt it useless to go further.

Another instance of the lack of appreciation and realization of the most important powers which the physician can exert is the manner in which some of our colleagues tend to look upon the modern revival of interest in the analysis of the mental phenomena of disease and the more studied application of psychical methods of treatment. They seem to regard the rather ponderous and impressive term "psycho-therapy" as the symbol of some wholly new and mystical method of influencing their patients.

But the awakening of interest in the study and application of psychical methods of treatment is important and hopeful—and not its least importance lies, perhaps, in the fact that we are reminded that many have forgotten to teach their students —some have failed to realize themselves—that by the mental control which we gain over our patients we can often accomplish more than by any other means.

The so-called "Christian Scientist" has discovered this, finds for himself a satisfactory explanation in his circumscribed religion, and with a simple ignorance of the elements of the natural sciences, constructs a grotesque system, which, while helping some, leads many astray.

Many of our so-called Homœopathic brothers must realize well that 'tis rather their confident assertions than their dilutions that tide their patients over the passing malady.

The quack, having made peace with his conscience, knows that, by his fantastic advertisements and ludicrous promises he will always gain the confidence of and actually help a sufficient number to keep his pocket padded—the main end of his existence.

The maker and advertiser of proprietary medicines knows that the false statements printed on his bottles inspire a confidence that is of benefit to some; that the statements are false, that they cruelly deceive many, he may, perhaps, fail to consider.

But the physician does not always realize that that which superstition and ignorance and ill faith may accomplish, he too can do equally well by properly directed effort, honestly and intelligently, and if you will, scientifically.

Just as it is true that the general practitioner is called upon, as a rule, to apply only the simpler forms of physical therapy, so it is with regard to methods of psychical treatment. In all those conditions in the treatment of which the mental influence of the physician on the patient is especially called into play, the individual is a most important factor, and it will probably always be the case, that in the graver nervous and mental maladies, the best results will be obtained by men especially gifted and specially trained. But many a patient might be saved from a long nervous breakdown or from the hands of the quack and the charlatan, if we were to remember, ourselves, and to teach our students to give more time and thought to the care of the mental attitude of the sick. An hour's patient attention and explanation and encouragement will often do more for the sufferer than months of routine treatment.

These, gentlemen, are the conceptions which I have wished to bring before you. They are neither new nor original, but they have, nevertheless, a bearing of some importance on the practice of medicine.

It is, of course, needless to add that, if I have insisted upon the value of more studied attention to physical and psychical methods of treatment, it is not that I would in any way detract from the value of drugs or deny the necessity of a thorough knowledge of their physiological action. Drugs are of course indispensable in the practice of medicine. To say that there are few specifics, and to warn against the indiscriminate use of substances of uncertain constitution, is far from denying the value of medicines. It is only by knowing how to take advantage of every current, to catch every passing breath of air, that the skilful yachtsman wins the race. The administration of a drug, intelligently, at the right moment and in the right manner, may tide the patient over the crisis which had otherwise been fatal. But it is none the less true that had it not been for other vitally important physical and mental measures this opportunity might never have been offered.

THE PHYSICIAN AND SURGEON IN SHAKESPEARE.

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"Under carved marble of thine own
Sleep, rare tragedian, Shakespeare sleep alone."
—*William Basse.*

To say that every genius has its satellites is but a very commonplace remark. Yet it is so easy to forget that the significance of many of these satellites has been misapprehended, that others have been completely forgotten, and that many more, no doubt, have remained as unnoticed upon the horizon of time as the stars by day, not even to be descried when the great central figure which eclipsed them was in its nadir. Thus it happens that the attention of posterity has been confined largely to the contemplation of the lives and the labors of its greatest forebears. The name of Hippocrates is daily on our lips, but the names of those who prepared the world for him and his labors and of those who immortalized him by their works, are often unknown to the tongues of men. In the words of Dr. Osler, "Such renown as they had, time has blotted out, and on them the iniquity of oblivion has blindly

scattered her poppy." It is the destiny of genius to involve its contemporaries in a partial, or, perchance, total eclipse. This has been true of the heroic figures in the arts of sculpture, painting, poetry, and music, as well as of those which have appeared upon the battle grounds of war and of philosophy. It was thus with Shakespeare. The wonder of a world is still upon him and his work, while his literary contemporaries receive but the attention of the student, the bookworm, or the lover of literature. This is inevitable. It is best that it should be so. Yet there is much indeed in the writings of these contemporaries which bears upon our theme. Even a few references will suffice to make this evident.

In an anonymous interlude, The Marriage of Witt and Wisdom, written in 1579, Idlenes, one of the characters representing vice, refers to the physician in no unequivocal terms. Idlenes declares:

> "Now am I nue araid like a phesitien.
> * * * * * * *
> Now shall you heare how findly Master Doctor
> Can play the outlandish man.
> Ah, by Got, me be the Doctor.
> Me am the fine knaue, *I* tell ye,
> And have the good medicine for the maiden's belly;
> Me have the excellent medicine
> For the blaines and the blister.
> * * * * * * *
> The bee have no so mony herbes
> Whereout to suck hony
> As I can find shifts whereby to get money."
> —*The Marriage of Witt and Wisdom*—Tertia Scena.

These lines were written only about twenty years before Henry V, Much Ado About Nothing, As You Like It, and The Merry Wives of Windsor, with its "Master Caius that calls himself Doctor of physic." The language used by Witt recalls that of John Heywood's "Poticary" rather than that of Shakespeare.

Most of the better-known Elizabethan dramatists had physicians and surgeons among their characters. In Chapman's All Fools, when a surgeon, Francis Pock, is called to care for a wound of the scalp, he gives a very cheering prognosis in the following words:

> "I'll make your head sound as a bell: I will bring it to suppuration, and after I will make it coagulate and grow to a perfect cicatrix, and all within these ten days, so you keep a good diet."—*All Fools*, III, 1.

Pock then wisely advises his patient, Dariotto, to come to his house so that the wound may be the better cared for.

Besides Dr. Faustus, who does not concern us, Marlowe introduces an apothecary and a surgeon into the Massacre of Paris. In Marston's drama, The Wonders of Women or the Tragedy of Sophonisba, written in 1606, there is one Gisco, a surgeon. Ford has one *true* physician (Corax) in The Lover's Melancholy, and a *supposed* physician (Richardetto) in another play, the title of which is not quotable. In Massinger's plays the medical profession is especially well represented—in numbers at least. The Duke of Milan contains *two doctors;* the Parliament of Love has a *court physician;* the Emperor of the East, a *surgeon* and an *empiric;* A Very Woman, one *physician,* two *surgeons,* and an *apothecary;* and the Bashful Lover, a *doctor.* In the works of Beaumont and Fletcher we have only a surgeon in The Chances, written by Fletcher, in 1617; but in Middleton's plays we meet quite an array of physicians, surgeons, and apothecaries. A Fair Quarrel contains a physician and a surgeon; The Family of Love has "Glister, a doctor of physic" and "Purge, a jealous apothecary"; The Changeling gives us "Alibius, a doctor who undertakes the cures of fools and madmen"; and finally in the Inner-Temple Masque there is Doctor Almanac. It is evident that there is no dearth of characters representing the medical profession in the plays of these contemporaries of Shakespeare. As to how well these physicians and surgeons represent, or misrepresent, their profession we cannot stop to consider. For, although interesting historically, as well as in connection with our theme, these delineations lack that greater claim which everything Shakespearean has upon us. The works of the above authors are not, as a rule, upon our shelves. Those of Shakespeare, on the contrary, maintain their time-honored place with the family Bible.

It is evident that as far as the number of the medical characters is concerned the plays of Shakespeare can have no claims above those of Massinger or Middleton. In Shakespeare there are seven physicians, but no surgeons or apothecaries. The last two professions are called into requisition only when the exigencies of the plays require it or they are retained from historical sources. Three of the seven physicians in Shakespeare's plays—the two doctors in Macbeth and the physician in Lear—remain anonymous. Those named are Cerimon in Pericles, Cornelius in Cymbeline, Caius in the Merry Wives of Windsor, and Butts in Henry VIII. The last four, and the physician in Lear, have each in turn suggested an historical personage *to someone.* The two doctors in Macbeth alone have withstood all speculation. Although Helena, in All's Well That Ends Well, is sometimes spoken of as a "woman doctor," and will be referred to again, she herself lays no claim to this title. She is, in the main, the prototype of Boccacio's Giglietta, and not a creation of Shakespeare. It is true, Lafeu announces her as a "medicine," but when she is presented to the king he declares:

> . . . . . "I say we must not
> So stain our judgment, or corrupt our hope
> To prostitute our past cure malady
> To empirics."
> —*All's Well That Ends Well*, II, 1, 122.

The words of the king quite correctly reflect the attitude of the Royal College of Physicians towards female practitioners. Queen Elizabeth's request, for example, made through her prime minister Walsingham, to let one Margaret Kennix, a poor woman, "to quietly practice and minister to the curing of diseases and wounds by means of certain simples, in the applying whereof it seemeth God hath given her an especial knowledge," was repeatedly denied by the College. Nevertheless, women practiced in Shakespeare's day, and we know that at earlier periods in the history of medicine—the Arabian—

matters pertaining to gynecology and obstetrics were exclusively in their hands.

Friar Laurence, too, must be excluded from the medical profession. He may be regarded as a last survivor of the monk-physician upon whom the Council of Tours set its ban in 1163; or better still, in spite of the slightly changed spelling of his name, as the exact Friar Lawrence found in Bandello's story of the same name. In this story we are told of Friar Lawrence that

"Not as the most was he, a grosse unlearned foole:
But doctor of divinitie proceded he in schoole.—l. 567.

* * * * * * * * *

The secretes eke he knew, in natures woorkes that loorke;
By magiks arte most men suppos'd that he could wonders woorke."—l. 569.

and that

"The bounty o' the fryer and wisdom hath so wonne
The townes folks herts, that welnigh all to fryer Lawrence ronne."

—*Tragicall History of Romeus and Iuliet*, l. 575.

The English doctor in Macbeth speaks but four and a half lines. He reveals a belief in witchcraft, so common at that time, and apotheosizes the cure, by the touch, by Edward the Confessor, of that which was the "mere despair of surgery"—the King's Evil. This doctor correctly represents many even famous physicians of the Elizabethan age in his belief that

". . . . . there are a crew of wretched souls
That stay his cure; their malady convinces
The great assay of art; but at his touch—
Such sanctity hath heaven given his hand—
They presently amend."

—*Macbeth*, IV, 3, 141.

This *English* doctor deserves no further comment, although he is repeatedly spoken of as "a noble doctor" by various writers. It is evident that his nobility rests on very meager facts. His colleague, the *Scotch* doctor of the same play, scarcely has a more important role. He is shrewd but tactless and shows a mercenary spirit. In the sleep-walking scene in which he says, "I will set down what comes from her [Lady Macbeth], to satisfy my remembrance the more strongly," he clearly shows his caution. Upon recognizing that "the great perturbation in nature," which afflicts Macbeth, is due to "unnatural deeds" which "breed unnatural troubles," he concludes that such a disease is beyond his practice. Nevertheless, Lady Macbeth's gentlewoman is commanded to

". . . . . look after her;
Remove from her the means of all annoyance,
And still keep eyes on her."

—*Ibid; vide infra.*

With this and with the words,

". . . . . More needs she the divine than the physician."

—*Ibid; vide infra.*

he leaves his patient for the night, without making any attempt to relieve or to end the somnambulism. Surely, he must have known as well as the physician in Lear, that "there is means" to "knit up the ravelled sleave of care." When a little later, in reply to Macbeth's remonstrance:

"Canst thou not minister to a mind diseased,
Pluck from the memory a rooted sorrow,
Rage out the written troubles of the brain,
And with some sweet oblivious antidote
Cleanse the stuffed bosom of that perilous stuff
Which weighs upon the heart?"

he bluntly answers,

"Therein the patient
Must minister to himself."

—*Macbeth*, V, 3, 46.

Macbeth justly resents this unfeeling reply with the familiar words,

"Throw physic to the dogs, I'll none of it."

We all symphatize with Macbeth in his solicitude for his wife and in his reproach of the physician, but we must remember that the circumstances in the play call for retributive justice and that in the requirements of the plot and not in the doctor's ability or character, least of all in the poet's opinion of medicine, lies the explanation of the doctor's reply. The plain professional duties of the physician are sacrificed that the ends of the drama may be fulfilled. After putting on his armor, Macbeth in his despair appeals to the doctor again.

"If thou couldst, doctor, cast
The water of my land, find her disease
And purge it to a sound and pristine health,
I would applaud thee to the very echo
That should applaud again."

—*Ibid.*

This cure is impossible, of course, for Scotland's disease is Macbeth himself. Consequently the prudent doctor gives an indifferent answer, but then makes that damaging admission:

"Were I from Dunsinane away and clear
Profit again should hardly draw me forth."

—*Macbeth*, V, 3, 61.

Danger to both person and reputation may excuse, to some extent, the doctor's desire to get away from Dunsinane, but certainly nothing can excuse the confession that profit drew him forth in the first instance. Yet he, too, has been judged a "noble doctor." The cupidity shown by him stands in marked contrast to the noble charity of Cerimon or to that of the physician referred to by Bassanio, in the Merchant of Venice, as

"A civil doctor
Which did refuse three thousand ducats of me."

—*Merchant of Venice*, V, 1, 210.

While Macbeth's appeals for Lady Macbeth and for "his land" remain unanswered, not so Cordelia's hopeless words respecting her demented, old father. Cordelia, lamenting, asks the physician,

"What can man's wisdom
In restoring his bereaved sense?"

—*King Lear*, IV, 4, 8.

and generously pledges,

"He that helps him take all my outward worth."

Here the physician's reply, in marked contrast to that of the doctor in Macbeth, is given in sympathetic words of hopefulness:

> "There is means, madam;
> Our foster nurse of nature is repose,
> The which he lacks; that to provoke in him,
> Are many simples operative, whose power
> Will close the eye of anguish."
>
> —*King Lear*, IV, 4, 11.

We next meet this physician in Lear's tent in the French Camp. While Lear, "that ruined piece of nature," lies asleep, soft music is playing. As the king stirs, the physician bids Cordelia come nearer and orders the music to sound louder. When finally Lear awakens, Cordelia is wisely asked to speak to him because "'Tis fittest." But the brain-sick old king is confused and so the physician counsels "He's scarce awake, let him alone awhile." Evidently the drugs and rest are supposed to have restored Lear's "bereaved sense," for the physician consolingly says to Cordelia:

> "Be comforted, good madam; the great rage,
> You see, is kill'd in him: and yet it is danger
> To make him even o'er the time he has lost,
> Desire him to go in; trouble him no more,
> Till further settling."
>
> —*King Lear*, IV, 7, 78.

The fact that this physician has music to sound during Lear's awakening is usually given as one of the evidences that Shakespeare was several centuries in advance of the physicians of his own time in his treatment of insanity. I do not wish to stop for a full discussion of this entire subject, but it must be admitted that undue emphasis has been laid upon this fact. In the 16th century music—such as it was— was very popular. Barbers had citterns and virginals in their shops for the amusement of their patrons. Ben Johnson refers to this custom in Every Man in His Humour, when he says, "I can compare him to nothing more happily than the barber's virginal; for every man may play upon him." Lanier gives a similar explanation for the connection between music and dentistry, in the following words:

> "If Shakespeare had wanted a tooth drawn he would have gone to the barber shop to get it done. And he managed to connect this uncomfortable profession with music by the singular custom which prevailed among barber dentists, of tying the teeth which he had drawn to the end of lute strings and hanging them in the window of the shop."
>
> *Shakespeare and His Forerunners*, Vol. II.

That music was used on many occasions we well know. It was used, for example, to stimulate the insane and idiots into all manner of antics, and as an accompaniment in teaching these unfortunates to dance for the amusement of others. Isabella, the wife of Dr. Alibius, who is the caretaker of fools and madmen in Middleton's play—The Changeling, rightfully says of this practice:

> "Alack, alack, it is too full of pity
> To be laughed at!"
>
> —*The Changeling*, 1633, III, 3.

Lollio, the assistant of Dr. Alibius, who conducts this performance, uses a whip in training the insane to keep them at a proper distance. The doctor tells us that he himself must be busy training the "brainsick patients" to perform at a prospective wedding

> ". . . . to make a frightful pleasure.
> To finish as it were, and make the fag
> Of all the revels, the third night from the first."
>
> —*The Changeling*, III, 3.

He then tells Lollio that he will see the final rehearsal and orders the madman hence with:

> "Away, rascal! I'll prepare the music, Lollio."

When finally Isabella, the doctor's wife, and Lollio, the keeper, re-enter with fools and madmen who dance, Dr. Alibius exclaims in glee,

> "Good boy, Lollio!
> 'Tis perfect: well, fit but once these strains,
> We shall have coin and credit for our pains."
>
> —*The Changeling*, IV, 3.

In The Chances, written by Fletcher, we see music used on a still different occasion. When Antonio, a patient, has his wounds dressed by the surgeon, he asks for both instrumental and vocal music besides wine and some other unspeakable thing. The First Gentleman says to Antonio,

> "Leave these things,
> And let him open you."

To which Antonio replies,

> "Do you hear, surgeon,
> Send for the music: let me have some pleasure
> To entertain my friends (besides your salads,
> Your green salves, and your searches) and some wine, too,
> That I may only smell it; or by this light,
> I'll die upon thy hand, and spoil thy custom!"

The First Gentleman commands,

> "Let him have music."
>
> —*The Chances*, III, 2.

After the surgeon's protest against wine is emphasized by the Second Gentleman, he asks Antonio, "Will these things please you?" Antonio replies:

> "Yes: and let them sing
> John Dorrie, ... I'll have John Dorrie!
> For to that warlike tune I will be opened."
>
> —*Ibid.*

That music was supposed to have strange and wonderful powers from time immemorial we all know. The Pied Piper of Hamelin, the story of David and Saul, and the Tale of King Eric of Denmark are well-known examples. Then, of course, there are the *reported* cures by the ancient Greeks and Romans of quartan fevers, the plague, syncope, insanity, epilepsy, deafness, serpent bites, and many other affections, through the use of wind instruments, especially the flute.

The physician in Lear is usually cited as the first reputable one in the plays of Shakespeare. Since King Lear was written in 1607, the year of the marriage of Susannah Shakespeare to Dr. John Hall, it is thought by some that Shakespeare in his portrayal of the physician in Lear meant to pay a tribute to his famous son-in-law. Be that as it may, there is no internal

evidence to that effect, and, of course, it is impossible to disprove the assertion. Furnivall and Lanier, however, think that Cerimon, in Pericles, represents Dr. Hall. If Pericles was written in 1609, as Knight, Meres and others hold, this is possible. If, as seems unlikely, "Shakespeare's own Muse her Pericles first bore," as Dryden says, and as Malone and Chalmer thought, then Cerimon manifestly cannot represent Dr. Hall.

Regarding Cerimon, Lanier very interestingly writes: "It is very delightful to think that this superb portraiture of the ideal doctor which Shakespeare has given us in the figure of Cerimon—a portraiture which ought to be in gold letters and framed and hung up in every medical college in the land—was possibly drawn from an actual personage. We know historically that in the year 1607 Dr. John Hall married Shakespeare's youngest daughter, Susannah. Now, Shakespeare's part of the play of Pericles was probably written just about this time, and it seems very likely that this son-in-law, Dr. John Hall, furnished him with at least some of the features which go to make up the noble Dr. Cerimon." Cerimon, it will be remembered, is the only physician of noble rank in the plays of Shakespeare. He is addressed by Pericles himself as "reverend appearer" and "Lord Cerimon." However, when we first meet him reviving the unfortunate Thaisa, he reminds one somewhat of a magician. His language is strained, and there is an air of mystery about him. Dowden, too, speaks of "Cerimon, who is master of the secrets of nature," liberal in his "learned charity," and "like a first study of Prospero—the great enchanter." Still we must not dismiss him thus. His speech and conduct are truly noble. We recall that when one of the shipwrecked gentlemen, after accosting Cerimon, exclaims:

> "But I much marvel that your lordship having
> Rich tire about you, should at these early hours
> Shake off the golden slumber of repose."
>
> —*Pericles*, III, 2, 21.

Cerimon reveals his nobleness in the reply:

> "I hold it ever that
> Virtue and cunning were endowments greater
> Than nobleness and riches;
> I have ever studied physic,
> Through which secret art—
> By turning o'er authorities—
> I have (together with my practice) made familiar
> To me and my aid, the blessed infusions
> That dwell in vegatives, metals, stones;
> And I can speak of the disturbances
> That nature works and of her cures, which doth give me
> A more content in course of true delight
> Than to be thirsty after tottering honour
> Or tie my treasures up in silken bags
> To please the fool and death."
>
> —*Pericles*, III, 2, 30.

The truth of these words is attested by the Second Gentleman in the words:

> "Your honour has through Ephesus pour'd forth
> Your charity, and hundreds call themselves
> Your creatures, who by you have been restored:
> And not your knowledge, your personal pain, but even
> Your purse, still open, hath built Lord Cerimon
> Such strong renown as time shall never. . . . ."
>
> —*Pericles*, III, 2, 43.

This splendid speech is unfortunately interrupted by the entrance of several servants carrying a box, "caulked and bitumed," which contains the unfortunate Thaisa. After hearing the story of the finding, Cerimon strangely enough, for a physician, at once thinks of gold!

> ". . . . . Whate'er it be
> 'Tis wondrous heavy. Wrench it open straight:
> If the sea's stomach be o'ercharged with gold,
> 'Tis a good constraint of fortune it belches upon us."
>
> —*Pericles*, III, 2, 54.

Why Cerimon, a rich man and a physician, should first think of gold as contained in the box is hard to understand unless it was due to a desire of "preserving life in medicine potabile"—the aurum potabile of the old physicians. This belief in the marvelous powers of soluble gold which, of course, they did not have in Shakespeare's day, is also referred to by the king in All's Well That Ends Well, when he observes:

> "Plutus himself,
> That knows the tinct and multiplying medicine,
> Hath not in nature's mystery more science,
> Than I have in this ring."
>
> —V, 3.

Were Cerimon not a philanthropic gentleman of fortune, Chaucer's lines:

> "And yet he was but easy of dispence,
> He kept that he won in pestilence,
> For gold in physic is a cordial;
> Therefore he loved it in special."

might contain an explanation. The above, however, seems the real reason, although Cerimon's surmise may be only indicative of the spirit of the times—times when treasure-trove and the philosopher's stone were the goal of many common folk, mariners and kings. The New World with its stories of fabulous treasure formed but a part of all this, and these things may explain the physician's remark.

When the box is opened, Thaisa is seen,

> "Shrouded in cloth of state, balmed and entreasured,
> With full bags of spices."

Cerimon now displays his self-possession and ability. Upon descrying life he orders a fire built, sends for his boxes, and commands,

> "The rough and woful music that we have
> Cause it to sound, beseech you
> The viol once more: how thou stirr'st, thou block!
> The music there! I pray you, give her air."

When Thaisa recovers, silence is ordered, and she is carried to a neighboring chamber where

> "The matter must be look'd to,
> For her relapse is mortal. Come, come;
> And Aesculapius guide us."
>
> —*Pericles*, III, 2, 109.

In the closing scene, in which Cerimon returns to Thaisa her jewels, suggests Diana's temple as a refuge, and offers his niece as attendant, he shows himself noble beyond compare. His generous invitation to Pericles to come to his house and "see all" ends the story.

Shakespeare's Cerimon, from Pericles, written in 1609, stands in marked contrast to the physician in Middleton's A Fair Quarrel, written in 1617. The latter wins his patient's confidence by telling her that

> "The patient must ope to the physician
> All her dearest sorrows: art is blinded else,
> And cannot show her mystical effects.
>
> * * * * * *
>
> If you knew well my heart, you would not be
> So circular; the very common name
> Of physician might reprove your niceness;
> We are as secret as your confessors,
> And as firm obliged; 'tis a fine like death
> For us to blab."
>
> —*A Fair Quarrel*, II, 2.

Jane, the patient, then confides in him, only to see him turn a perfidious tempter. When he has threatened his worst regarding her conduct, she defies him in a severe but just denunciation:

> "Away, you are a blackamoor!
> . . . . . Are you the man
> That in your painted outside seemed so white?
> O you're a foul dissembling hypocrite!"
>
> —*A Fair Quarrel*, III, 2.

Cornelius, the physician in Cymbeline, is supposed to be taken from Cornelius, the physician to Charles V. The latter is said to have gained great repute all over Europe by curing the emperor of gout and general debility. When the treacherous queen, in Cymbeline, applies to Cornelius for poison to administer to Imogen, under the plea that she wishes

> ". . . . to try the forces
> Of these compounds on such creatures as
> We count not worth the hanging, but none human."
>
> —*Cymbeline*, I, 5, 18.

Cornelius discourages her by declaring,

> "Your highness
> Shall from this practice make hard your heart,
> Besides, the seeing these effects will be
> Both noisome and infectious."
>
> —*Cymbeline*, I, 5, 24.

But Cornelius, who suspects the designs of the queen, instead of poison

> ". . . . did compound for her
> A certain stuff, which being ta'en would cease
> The present power of life, but in short time
> All affairs of nature should again
> Do their due functions."
>
> —*Cymbeline*, V, 5, 254.

So far, Cornelius shows compassion, prudence, and good judgment. However, like the Scotch doctor in Macbeth, he later receives a just rebuke. When Cymbeline is in his tent surrounded by victorious followers to reward his heroes, Cornelius, accompanied by women, enters the tent. As the king sees them, he surmises:

> "There's business in these faces. Why so sadly
> Greet you our victory?"
>
> —*Cymbeline*, V, 5, 23.

To this Cornelius bluntly answers,

> "Hail, great king!
> To sour your happiness, I must report
> The queen is dead."
>
> —*Cymbeline*, V, 5, 26.

The outraged feeling of the king finds expression in the rebuke:

> "Who worse than a physician
> Would this report become? But I consider
> By medicine life may be prolong'd, yet death
> Will seize the doctor too. How ended she?"
>
> —*Ibid; vide infra.*

Cornelius then tells the iniquitous story in all its tragic details. He spares the king not one iota, but unfeelingly tells of the homicidal designs of the disloyal queen who repented

> "The evils she hatch'd were not effected; so
> Despairing died."
>
> —*Cymbeline*, V, 5, 59.

The physician in Henry VIII, Dr. Butts, has no professional rôle, but simply calls the king to witness the humiliation of the Archbishop, Cranmer, before the council chamber. He is the prototype of the court physician of Henry VIII of the same name. In life, he sympathized with the Archbishop and sympathetically kept him company for a whole hour before the locked doors of the council chamber. It was to him that Dr. Caius, the founder of Caius College and second president of the Royal College of Physicians, dedicated most of his books. He was knighted by Henry VIII as Sir William Butts, and is said to have administered his gout powder—the raspings of a skull unburied—to the Merry Monarch himself. That he was held in high honor is well shown by the fact that his portrait is said to adorn the picture of the delivery of the charter to the surgeons' company in 1572. In the Annals of the Royal College of Physicians, he is recorded thus: "Vir gravis; eximia literarum cognitione, singulari judicio, summa experientia, et prudenti consilio doctor." Hence scant justice is done Dr. Butts in Henry VIII, where he plays a trifling and seemingly ungrateful rôle.

Of the irascible French physician, Dr. Caius, of The Merry Wives of Windsor, Hazlitt in his Character Studies of Shakespeare writes: "The duel scene with Caius gives him [Caius] an opportunity to show his valor and his melancholy in an irresistible manner. In the dialogue which, at the mother's request, he holds with his pupil, William Page, to show his progress in learning, it is hard to say whether the simplicity of the master or of the pupil is the greatest." Caius, as is familiar to everyone, takes no medical rôle. He is simply an indiscreet love-maker, a rival of the imbecile Slender, who uses amusing English, gets into a burlesque duel, is mocked and ridiculed by everyone, and ends by marrying—to quote his words—"un garçon, a boy; un paysan, by gar, a boy; not

Annie Page; by gar, I am cozened." That this "Monsieur Mock-water," as the Host calls him, cannot represent the wealthy and honored founder of Caius College would seem self-evident. Fortunately it is easy to separate the Caius of Shakespeare from the Caius of history. The historical Dr. Caius, a pupil and friend of Vesalius, started dissections of the human body in England, wrote "A Boke or Counseill against the Disease commonly called the Sweate or Sweatyng Sickness," and succeeded Linacre as second president of the Royal College of Physicians. To this office he was re-elected nine times. He died about 28 years before The Merry Wives of Windsor was written. His only epitaph very appropriately and strangely enough for that day reads, "Fui Caius. Vivit post funera virtus." In his Harveian oration Dr. Osler writes of him as follows: "The contemplation of such a career as that of Caius could not but inspire with enthusiasm any young man. No one in the profession in England had before that time reached a position which I may describe as European. An enthusiastic student and a friend of all the great scholars of the day; a learned commentator on the works of the Fathers; the first English student in clinical medicine; a successful teacher and practitioner; a keen naturalist; a liberal patron of learning and letters; a tender and sympathetic friend—Johannes Caius is one of the great figures in our history." Certainly Shakespeare's sense of justice would not have permitted such a travesty of so great a person, and we must conclude that no delineation of this learned man was intended in The Merry Wives of Windsor.

That the French physician, Turquet de la Mayerne, Baron of Aubonne, who came to England in 1607, could not have been meant, seems equally certain. This unfortunate man had been persecuted by his fellow Frenchmen, partly because of his religion, but mainly because he favored some drugs condemned by the Paris College of Physicians. This college in 1603 forbade any of its members to consult with Dr. Mayerne because he espoused the doctrines of Paracelsus. Consequently he left France, came to England in 1607, and gained immediate fame. He compiled the first pharmacopeia published by the Royal College of Physicians, and through his influence at court achieved the separation of apothecaries and grocers. In England he was known as Sir Theodore Mayerne and was court physician to James I and his queen until James's death. After this he became physician to Charles I. Before coming to England he had also been physician to Henry IV of France. He had studied at Heidelberg and Montpelier, and was an authority on distillations. At his death in 1655 he is said to have left a large fortune.

It is not at all unlikely that the introduction of the comical Frenchman, Dr. Caius, into The Merry Wives of Windsor was due to the same impulse which prompted Middleton to introduce into A Fair Quarrel a nurse who betrays her German ancestry by the broken English which she uses. It was the custom to introduce comical characters into plays. They served as mere diversions. Brandes gives the following very satisfactory explanation for the introduction of Dr. Caius into The Merry Wives of Windsor. Brandes observes that "Shakespeare had just been trying his hand in Henry V at writing broken English spoken by a Welshman and by a Frenchman. He knew that at court where people prided themselves on the purest pronunciation of their mother tongue, he could find an audience exceedingly alive to the comic effects thus obtained, and he therefore, while he was in the vein, introduced into this hasty and occasional production two not unkindly caricatures—the Welsh priest, Sir Hugh Evans, in whom he probably immortalized one of his Stratford schoolmasters, and the French Dr. Caius, a thoroughly farcical eccentric who pronounces everything awry."

It was not the character of the Elizabethan age to exalt the surgeon and surgery, yet great advances were made in surgery during those days by men who are famed for all time. In fact, surgeons could not get even simple justice. Their position was not an enviable one. They had to struggle against the prejudices and open opposition of physicians, and were not permitted to free themselves from that incubus—the barber. The fact that most surgeons, no matter how learned, usually wrote in the vernacular drew down upon them the wrath of the physicians. They were accused of giving away the secrets of the profession and were often persecuted maliciously No lines of demarcation between the provinces of the physician and the surgeon existed. Surgeons usually wrote on medical topics also. William Clowes, the surgeon to his majesty, for example, wrote on "lues venera," as did many other surgeons, notably Pare. Woodhall has a chapter on scurvy; and nearly all surgeons—very naturally in those days—wrote on the plague.

In the dramas written by the contemporaries of Shakespeare, mentioned in the beginning of this article, the physician and surgeon are almost equally well represented. In the plays of Shakespeare we find no surgeon. Consequently for an estimate of him we must rely wholly upon the expressions of the various lay characters. Usually the surgeon is sent for in case of dire necessity. This occurs in Romeo and Juliet, Othello, The Merchant of Venice, Twelfth Night, Macbeth, and in Lear. Shylock, too, is advised to

> "have some surgeon . . . . to stop his [Antonio's] wounds."
> —*Merchant of Venice*, IV, 1, 257.

In Othello, Cassio replies to Iago's exclamation, "What, are you hurt, lieutenant?" with the words, "Ay, past all surgery." Cassio considers himself "past all surgery," not because of a mortal wound but because he has lost his reputation—a malady which defies the surgeon still. But not alone a blemished character was considered beyond the skill of the surgeon, for Lysimachus asks:

> "Have you that a man may deal withal, and defy surgeons?"
> —*Pericles*, IV, 6, 39.

Lysimachus here refers to lues. A similar instance is found in Macbeth. In this play, Malcolm speaks of

> "Strangely visited people
> All swollen and ulcerous, pitiful to the eye,
> The mere despair of surgery."
> —*Macbeth*, IV, 3, 152.

It was this affection, scrofula or the King's Evil, which was thought to yield to the royal touch alone. At that time, how-

ever, a variety of glandular affections, which have since been distinguished as separate diseases, were designated by this name. Even at the present, when we know "the ground whereon these woes do lie; the true grounds of all these piteous woes we cannot without circumstance descry." In those days, on the contrary, these very circumstances were unknown and consequently for this, and for other better reasons, no reflections upon the surgeon or surgery can here be intended.

There are many instances which illustrate well the necessity of reckoning with the character of the speaker and with the dramatic situation. Lear, that "sight most pitiful in the meanest wretch, past speaking in a king!" for example, calls for a surgeon because in his madness he thinks himself "cut to the brain." It would be foolish to conclude that suture of the brain was done in Shakespeare's time, and yet just such conclusions are repeatedly drawn by physicians of to-day. Likewise in Twelfth Night (V, 1, 202) the clown—but what doesn't a clown say!—when Sir Toby asks, "Sot, dids't see Dick Surgeon, sot?" replies, "Oh! he's drunk, Sir Toby, an hour agone; his eyes were set at eight i' the morning." No one should take Sir Toby's "Dick Surgeon" seriously. We all know Sir Toby. Dick Surgeon is polite language for him. It should also be noticed that Sir Toby turns the clown's thoughts to drunkenness by twice calling him "Sot."

It would be incorrect to say that, all in all, the surgeon is depreciatingly spoken of in the plays of Shakespeare. Although he is but incidentally referred to, yet the fact that he is "the brother of grim necessity" shows that his services were considered indispensable. It would be quite as easy to make out a vigorous case against the physician if we chose our references with that end in view. Perhaps if we hear the blame bestowed upon the latter we may the better appreciate the praises.

In sonnet 66, line 19, we meet with the simile: "Folly, doctor-like, controlling skill." The custom of giving hopeful prognoses in cases of extremity is ridiculed in sonnet CXL. Here we are told that

> "Testy sick men when their death be near
> No news but health from their physician hear."

In Lucrece "Advice goes sporting while the patient dies"; while Sempronius, in Timon of Athens, demands:

> "Must I be his last refuge?
> His friends like his physicians
> Thrice give him o'er."
> —*Timon of Athens*, III, 3, 11.

Sempronius here refers to the then still prevalent custom of abandoning all incurables to mountebanks lest failure to cure the patient injure the physician's practice.

Marcius makes a "lip at the physician" and flouts the value of the "most sovereign prescription of Galen." Likewise the wordy Lafeu, the old lord who speaks "special nothings," asks to be "relinquished of the artists." To this Parolles, that "good window of lattice," approvingly adds:

> "So, I say: both of Galen and Paracelsus."
> —*All's Well That Ends Well*, II, 3, 11.

If, as was so often the case, physicians had administered potions to Parolles and Lafeu which they would "tremble to receive" themselves, we can readily forgive the victims for their wishes. Indeed, we ought to forgive them if they had said severer things than these.

Most of us who know Timon know how to judge his warning:

> "Trust not the physician;
> His antidotes are poison and he slays
> More than you rob."
> —*Timon of Athens*, IV, 3, 436.

For the same reason weak King Richard's prayer does not disturb us. It was natural for this "unstaid youth" to pray,

> "Now put it Heaven into his physician's mind
> To help him to his grave immediately."
> —*Richard II*, I, 4, 59.

The sombre picture of the physician presented to us here is offset by many expressions of a wholly different character. Paulina, for example, implores Antigonus to hear her who professes herself

> "Your loyal servant, your physician."
> —*All's Well That Ends Well*, II, 1, 188.

The king, who previously referred to Helena as an empiric, later addresses her, "sweet practiser, thy physic I will try." Even Mrs. Quickly, the hostess of the Garter Inn, in her plain-spoken way, asks:

> "Shall I lose my doctor? No, he gives me the potions and the motions."
> —*Merry Wives of Windsor*, III, 1.

Again, Count Rousillon, the historic Gerhard de Narbonne, Helena's father, is justly referred to as one "whose skill was almost as great as his honesty."

> "Would for the King's sake he were living!
> I think it would be the death of the King's disease!
> —*All's Well That Ends Well*, I, 1, 24.

Strange enough it was he to whom Bertram referred when he scornfully said:

> "A poor physician's daughter my wife? Disdain
> Rather corrupt me ever."

Of course Bertram, the unwilling groom, was as wrong about Helena's father as he was regarding other physicians. Physicians were not poor, but received good fees, carried canes, wore high hats, dressed in velvet and wore specially decorated velvet caps, had valets, and frequently rode on horseback seated in a side-saddle.

It is apparent from the foregoing quotations that the picture of the physician and surgeon in Shakespeare is a composite one. In this it is true to life, for the medical profession in Shakespeare's day was composed of a motley company. Even a slight acquaintance with the medicine of the 16th century and with the physicians contemporary with Shakespeare makes this evident. As a class, physicians were ignorant, superstitious adherents to the past who did not believe their own eyes. Yet there was no dearth of men renowned, for all time, for their professional ability, for their achievements and for their character. Their names are cherished and their labors highly regarded by physicians of to-day. It is these physicians and

surgeons who must be our guides in critically judging the delineations of the doctors in the plays of Shakespeare. As we saw, the physicians in Shakespeare are minor characters who have little opportunity to display professional knowledge, and often form but a small though indispensable part of the dramatic machinery. Their speech, which is not at all characteristic of their profession, is usually determined by the course of events beyond their control. Their character, in several instances, is not above reproach, but we must bear in mind that their sins of omission and commission are frequently the inevitable results of circumstances. Hence we must not judge them apart from their dramatic relations. As we have seen, a few of them may represent personages from actual life. If so, they do it very inadequately, however, for there is no agreement among critics on this matter, save in the very apparent case of Dr. Butts.—There could not well be any disagreement regarding him.

It is idle to theorize, yet it seems that had Avon's bard intended to pay a tribute to the doctors of his time or to those of any other time, he could not have allotted minor rôles to all of them. This seems self-evident, if we recall how many of the physicians of Shakespeare's day struggled so heroically, though of necessity so hopelessly, with the ravages of the sweat and the plague, and how they remained to care for the afflicted and the dead until they themselves fell victims to these scourges. Pepys, in an entry in his diary, made on October 16, 1665, during the great plague of London, refers to these conditions by saying, "And they tell me that, in Westminster, there is never a physician . . . . left, all being dead." From such and from many other facts and from the names of illustrious physicians and surgeons, which are revered to this day, it is plain that there was no dearth of material for the portrayal of the physician in a leading rôle by the world's greatest dramatist. Since his muse knew no bounds there are those who have asked why this was not made. It profits little to speculate. Shakespeare was great and Shakespeare was human. These are two potent reasons why he did some things and left others undone. As for myself, I prefer to take refuge, concerning such matters, in Gothe's wise words of counsel:

> Grau, theurer Freund, ist alle Theorie,
> Und grün des Lebens goldener Baum.
> —*Mephistopheles to the Student, Faust.*

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(14) Further references to the literature used will be found in an article, by the author, in the Johns Hopkins Hospital Bulletin, Vol. XVIII, No. 190, January, 1907.

[1] All references to Shakespearean plays are based on the International Shakespeare, published by the University Society, New York, 1901.

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EPIDEMIC PNEUMONIA.

By Marshal Fabyan, M. D.,

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From time to time cases of pneumonia have been reported occurring in groups, and not only has this happened too often to be explained by independent infections in every case, but such epidemics are sufficiently rare to make it worth while to report them. These groups may include two or three persons and be associated with some room or house or may be widespread, involving cities and districts.

The more important of these epidemics occurring between 1873 and 1903, have been recorded by Wells. Several plagues of earlier years, said to be a form of pneumonia, are too doubtful to be considered.

The frequent reports of several cases of pneumonia occurring in limited areas and in rapid succession has gradually led to the opinion that pneumonia is far more contagious than is generally supposed. That there are undoubted cases due to direct contagion cannot be questioned .

Osler reports an instance in which ten occupants of one house were attacked. He has seen three members of a family consecutively attacked with a most malignant type of pneumonia.

Müller stated that in the house of a poor village watchman three members of a family of four, and two visitors were affected one after another.

Ritter observed an epidemic of five cases in one house; twelve days later two others working in the house developed pneumonia.

Netter has reported several interesting cases. In one, a son, who was convalescing from acute articular rheumatism, developed pneumonia, from which his father was suffering.

Wilson reported the case of a man who, nineteen days after an attack of pneumonia, had a reinfection of the same lobe (right lower). His brother who nursed him developed pneumonia five days later. A college mate who went into the room of the first man developed the disease two days later. All were cases of typical croupous pneumonia.

Banks, of Chicago, records four consecutive deaths from pneumonia in one family and six among the friends who attended the funerals.

Tucker describes the disease occurring in a colored family in poor sanitary conditions. A sickly, seventeen-year-old daughter was the first to be taken ill; the mother became exhausted nursing her daughter and was the next to contract the disease. The pulmonary area involved was lobar in type; both patients died. Within forty-eight hours, four other members of the family between three and thirteen years of age were taken ill, and the course of the disease in these cases was prolonged.

Other cases are considered to be due to infection from animals, especially parrots. In 1892 a serious and important epidemic of fever associated with pneumonia occurred in Paris which was traced by Nocard to infection with a bacillus which causes the disease *Psittacosis* in parrots. This bacillus belongs to the general class of paracolon, and the disease developed with diarrhœa and headache, simulating typhoid fever, together with more or less pulmonary involvement.

Certain articles from the sick-room seem able to transmit the contagion. Flindt reports a case in which the coverings of a bed in which a pneumonia patient died were carried to a house two miles away and, four weeks later, used on the bed of a child, who promptly developed pneumonia. Another child developed pneumonia three days after his father started to repair a chair which was being used by a patient convalescing from pneumonia.

The spread of pneumonia in institutions and cities is only another form of these epidemics. In hospitals bed to bed infection, or the development of several cases in one ward, has suggested the contagiousness of pneumonia, but with ordinary precautions there seems to be very slight danger. A. H. Smith records one case in which the nurse died of the infection caught from her patient. Girdiner reports a second one. Edsall and Ghriskey record a severe case of pneumonia which ended fatally; the two patients who next occupied the bed had mild attacks; two others in nearby beds developed pneumococcal infections; still another case occurred soon after, perhaps by contagion. Upon thorough disinfection no other cases developed.

Tyson describes an epidemic in which 410 members of a ship's crew were attacked in rapid succession; of 720 men affected, 298 died. On the ship St. Jean d'Acre, of a crew of 815 men, 410 were attacked and those transferred to the Malta hospital communicated the disease to some of the inmates.

Emmerich describes an epidemic in the prison at Amberg in 1880, which lasted six months; of 161 cases, 40 died. The pneumococcus was isolated from the dust under the floor of the infected dormitory; it was not found under the others. Disinfection put an end to the epidemic.

Napier reports a pneumococcal septicæmia which proved very fatal to the men in the Johannesburg ruins. Rhinitis, basal meningitis, pneumonia, and a general septicæmia were present. The pneumoccus was found throughout the tissues post mortem.

Blyth calls attention to the contagiousness of pneumonia in certain English villages in 1875. Butry also describes an epidemic which was spread by friends visiting patients in a hospital. In 1888 Ballard described the Middleboro Epidemic in which 367 cases occurred in a population of 40,000 people. He considerd the pneumonia in these cases as septic in origin, arising from poisonous meats (bacon).

During the building of the new Croton Aqueduct in New York in 1886, Darling treated 150 cases among the poorly housed Italians. Rodman, of Frankfort, Kentucky, reported

in one year 118 cases with twenty-five deaths in a population of 735 persons.

Some consider the cases of pneumonia above described to be of the ordinary croupous type, which have spread under especially favorable conditions, as, for example, lowered vitality of the individual, exposure to storms, cold, privation, exhaustion, and even prolonged sleep (!).

The predisposing influence of other diseases, such as whooping-cough and measles, is well known. An exceptional virulence of the pneumococcus may be an important element. Others have considered epidemic pneumonia as an entity, even going so far as to give it a separate symptomatology and pathology. In favor of the former idea is the fact that in epidemics the individual cases have run a course altogether similar to that of a croupous pneumonia, with the ordinary mortality. In one epidemic the change in virulence was interestingly followed; the attacks began in the summer with a few cases in which the symptoms and course were indefinite, although large numbers of pneumococci were found in the sputa. The symptoms gradually became more definite and the course more severe until, in February, one woman died of definite lobar pneumonia in forty-eight hours.

Aufrecht, in Nothnagel's encyclopedia, treats of epidemic pneumonia under the heading of Atypical Pneumonia, and Wells has called attention to certain individual peculiarities which seem to characterize special epidemics.

On March 24, 1906, a series of five cases of pneumonia occurring in a colored family, entered the Johns Hopkins Hospital, and it was with the hope of determining the ætiological factors in this particular epidemic, that this study was undertaken. The important facts of the cases were as follows:

The family consisted of a father, mother, and eight children, four boys and four girls, between the ages of two and seventeen years. The oldest, a girl, lived out, and seldom visited the family. The rest lived in an old dilapidated wooden house, one and a half stories high, which was located in an outlying district of Baltimore with no buildings in the immediate neighborhood. It stood back from the road, in the gutter of which ran dirty water, and was separated from a brewery by a long gentle slope. An ordinary privy was distant about fifty feet.

The lower floor of the house was divided into an unused room and kitchen on the back, and a cold, cheerless guest room and a living-room on the front. Patients I and V slept in the guest room up to within two weeks of the first illness, when they moved to an unheated garret room containing only a cot. The living-room downstairs was neat in appearance, about 20 x 15 x 8 feet, with two doors and two windows. In one corner the father, mother, patient III, and occasionally patient II slept in a bed. In a cot in another corner patients II and VI usually slept, and another cot was occupied by patients IV and VII. At night the only ventilation was by cracks, and a small stove burnt continually.

Six months before the patients entered the hospital patient VI suffered from a severe attack of whooping-cough, and patient III also developed a mild attack. The other children, except patient V, developed coughs at this time, but never whooped, according to the mother, and continued at school, where there were known to be other cases of whooping-cough.

The children had not recovered their former strength nor were they entirely free from cough when, about March 8, the father stopped work at noon for a few days on account of a cold, hoarseness and "misery" in the stomach. He suffered no pain in the side, dyspnœa or cough; he does not think that he had fever. An examination of his chest two weeks later disclosed nothing abnormal.

Three days later (March 11), patient I felt sickly, but did not go to bed until four days afterwards, complaining of a chill, pain in the stomach, and shortness of breath. Her abdomen gradually became extremely tender. The bowels, which had been regular, were constipated for two days, and later, after taking medicine, the stools became frequent, watery, and of a yellow color.

The day before patient I went to bed (March 14), patient II began to complain of epigastric pain and developed a cough and some pain in the side. She was very sick for two or three days, short of breath and fretful, but was about the house when the others were sent to the hospital, and remained at home. An examination of her lungs showed a resolving pneumonia at the base behind.

Three days later (March 17), patient III complained of pain in the stomach. The next day patient IV had epigastric pain and shortly afterwards a pain in his side. The following day patient V was taken sick with similar symptoms and a chill.

Two days later (March 21), patient VI became ill. A few days later patient VII complained of headache and stomachache, but was about as usual after a few days in the house. A week later his lungs appeared normal. The mother nursed all the children and remained perfectly well. The oldest daughter also helped with the nursing for the three days preceding the admission of the patients to the hospital but remained well. So far as known, there was no sickness in the guano factory where the father worked, or in the neighborhood of the house, which had been very free from disease. There had been no animal pets in the house. No unusual articles of diet had been indulged in, and only city water was drunk. There was no sickness in the family whose washing the mother did. Second-hand blankets were purchased about March first from a dealer, who had procured them in a barrel of unclaimed freight from the railroad. As auctions of this freight only occur every few years, and as the law will not allow a sale until the article has been held at least a year, it does not seem probable that these could have been the source of the infection. Moreover, they were well washed before being used on the children's beds. The sputa is said to have been deposited on rags or in a spittoon.

Patient VI, who suffered most severely with whooping-cough, had only a mild attack of pneumonia and was the last to become affected, although he slept with his sister, who

was the second to develop the disease. A similar instance occurred three days apart. The onset was sudden, usually at night, and associated in two instances with a chill. All had practically the same symptoms: Headache, pain in the epigastrium and chest, with cough. All but one developed diarrhœa.

The following is an abstract of the notes made on admission to the hospital, March 24:

CASE I.—Colored female, 14 years old; occupation, housework. Complaints: Sore throat, pain in the stomach and chest of seven days' duration. There was a distant family history of tuberculosis, but the previous health of the patient had been very good. She had raised considerable frothy and blood-tinged sputa in the present illness.

On physical examination restlessness and dyspnœa were marked. Alæ nasi, active. Respirations, grunting. Patient cried out from pain in the right chest. Sclerotics, jaundiced. No herpes. Tongue, heavily coated. Pulse, regular, 132 per minute, of good size and fair tension (105 mm. of Hg.), not dicrotic.

Thorax.—Well formed. Breathing, costo-abdominal, short, jerky and rapid. Well marked consolidation of the left upper lobe with some involvement of the lower was made out, together with a pleuritic rub over the right lower front. The heart was apparently of normal size, and the sounds clear, the second pulmonic being markedly accentuated. The abdomen was slightly full. The walls were held rigidly, though no muscle spasm could be made out. General abdominal tenderness. No peritoneal friction elicited. Hepatic dulness reached to the costal margin. The rest of the examination was not remarkable. The expectoration was moderate in amount, frothy, mucopurulent and blood-tinged.

The blood examination showed a white count of 29,200 cells and a slight anæmia.

Urine.—Dark, 1015; albumin, trace; sugar, absent; no casts; bile reaction, present; diazo, absent.

The patient became deeply comatose, with the signs of consolidation more distinct at the left base and beginning involvement of the right base. Death occurred quite suddenly three days after admission, probably the eleventh day of the disease.

The blood cultures showed the presence of the pneumococcus.

Diagnosis.—Acute lobar pneumonia. An autopsy was performed by Dr. Cullen.

Anatomical diagnosis.—Acute pseudo-lobar pneumonia; acute fibrino-purulent pleuritis; pericarditis; diaphragmatic pleuritis and general peritonitis; acute splenic tumor; cloudy swelling of the viscera; lymphatic hyperplasia of the ileum; acute mesenteric lymphadenitis.

Lungs.—The left was voluminous, the lower portion being firmly bound to the diaphragm by a thick tenacious exudate. Palpation revealed many firm nodular areas throughout the lung. On section the surface presented a mottling of grayish-red, opaque, slightly elevated areas, alternating with depressed areas of a rather dark red color. This condition was most marked in the upper lobe, but was also present to some extent throughout the lower lobe.

The right lung appeared to be more air-containing than the left. On section it was atelectatic at the apex with slight mottling below, but no areas of nodular thickening were made out. The injection of the bronchi was more marked than on the left.

Microscopically, the lungs presented definite areas of broncho-pneumonia. Many alveoli apart from the bronchi showed some breaking down of the walls, but were free from exudate. Others near the bronchi showed typical red hepatization. In other sections the involvement was more general and mixed. Accumulations of leucocytes suggested purulent foci, but there was no definite relation to the bronchial wall. The rest of the necropsy was unimportant for the present consideration.

Cultures of the heart's blood and from the peritoneal cavity showed the presence of the pneumococcus.

CASE II had so far recovered that she was not sent to the hospital. Signs of a resolving pneumonia were present in the back at the time.

CASE III was a boy two years and eight months old. Except for an attack of summer diarrhœa two years before he had been in good health. On March 17 he became fretful and developed a paroxysmal cough and a fever.

On admission to the hospital, four days later, he was found to have rapid grunting respirations and a loose cough. The pulse was 136 to the minute, regular, and of good quality. Except for harsh breathing over the right front and a small area of tubular breathing inside the angle of the right scapula the right lung seemed normal. On the left there were suppressed breath sounds with prolonged expiration at the base of the axilla, with dulness, tubular breathing, and a few medium moist râles below the mid-scapular region. Heart, negative. The white cells numbered 39,000.

Five days after admission the temperature was normal, but rose slightly, and with flatness, diminished breath and voice sounds at the left base, an effusion was suspected. A needle was introduced with negative results. The white count reached 62,500 the following day and then slowly dropped. The patient was discharged two weeks after entrance with some impairment of resonance at the left base.

Diagnosis.—Acute lobar pneumonia. The child was sickly for some weeks after being discharged, but four months later appeared as well as before his illness.

CASE IV was a boy of seven years who complained of pain in the right side of three days' duration. Previously healthy. Physically, no discomfort. Pulse, 116 to the minute, regular, of moderate size and tension, not dicrotic. There was consolidation of the right upper lobe. Heart, negative. Abdomen, slightly full, tympanitic. Hepatic dulness reached one finger's breadth below the costal margin.

The blood examination showed a white count of 27,000 cells and a moderate anæmia.

Urine examination, negative. Diazo reaction, absent.

Four days after admission a crisis occurred and about five days later the lungs were clear. The white cells quickly dropped to 9000.

Diagnosis.—Acute lobar pneumonia.

CASE V was an orphaned cousin who lived with the family, a girl 15 years of age. She complained of pain in the side. The present illness began with a cold which was followed by a chill and cough with bloody expectoration. On admission, two days later, she did not look ill, but the respirations were quickened, and the alæ nasi were active. No herpes. Pulse, 88 to the minute, regular, of fair size and moderate tension. On respiration the right side moved more than the left. There was well marked consolidation of the right upper lobe. The heart was not enlarged and the sounds were clear. Pulmonic second sound accentuated.

The white cells were 19,050. Diazo reaction, absent. The leucocytes quickly dropped, and within a week, although there was dulness over the right apex, the breath sounds were clear. In another week all signs of consolidation had disappeared.

Diagnosis.—Acute lobar pneumonia.

CASE VI was a boy of six years who entered the hospital with the other cases, complaining of pain in the chest and a dry cough of one day's duration. He was restless and dyspnœic, coughing frequently. Herpes, marked. Tongue thickly coated. The pulse was 116 to the minute, regular in force and rhythm, of good

quality. The note over the left upper chest was duller than on the right and the breath sounds were harsh throughout, but nowhere tubular. A few râles were localized near the left nipple. Examination of the heart and abdomen proved negative. The white cells numbered 23,000. Urine examination negative.

Two days later there was a small patch of consolidation in the left lower front, but no further signs developed, and in two weeks the lungs appeared clear.

Diagnosis.—Acute lobar pneumonia.

Reviewing the above cases briefly, it is evident that the etiological factor which caused so many cases is obscure. The somewhat poor sanitary conditions and whooping-cough were assuredly predisposing causes, but the patient who had whooping-cough most severely, developed a very mild type of pneumonia after the others had succumbed.

Is there anything in these cases to suggest a spread from one bed fellow to another? Let us consider the situation.

In one bed slept father, mother, patient III (and sometimes patient II).

In one bed slept patients I and V.

In one bed slept patients II and VI.

In one bed slept patients IV and VII.

The first case of illness was in the father, a respiratory infection of doubtful nature; this was followed in six days by the illness of patient II, an occasional bed fellow, and in nine days by that of patient III, a regular bed fellow.

The second case of illness occurred three days later in the outbreak of patient I which was followed in eight days by the illness of his bed fellow (Case V).

The third case of illness was the outbreak of patient II, six days after the illness of his father, with whom he sometimes slept. This was followed in seven days by the illness of patient VI.

The outbreak of the fourth case of illness (Case III) has already been described as occurring nine days after the illness of his father.

The outbreak of the fifth patient (Case IV) occurred seven days after the illness of patient I, and was followed about a week later by the illness of his bed fellow (Case VII).

These figures are not uninteresting, showing, as they do in the more certain pneumonias, a period between the involvement of the original case and that of the bed fellow of just about a week in each instance. If we are to assume that the contagion spread from bed fellow to bed fellow and that the father's slight infection was the main origin of the epidemic, we may trace further a period of six days on the one hand and nine on the other, between his illness and that of his bed fellows (Case II and Case III), leaving the origin of Case I alone unaccounted for. It might not be going too far to assume that as the father's illness and that of patient I were separated by but three days, the source of infection was the same.

Interesting as these figures are, it must, however, be acknowledged that the weight of evidence appears to be in favor of a shorter incubation period in pneumonia. The blankets might have been a source of infection, but their previous history could not be obtained, while the length of time and thorough washing before using practically rules them out. The symptoms and signs were sufficiently typical to justify us in regarding the cases clinically as ordinary acute pneumonia, though certain features were noted peculiar to other epidemics, i. e., diarrhœa, protracted irregular fever, and jaundice.

The pathological findings in the lungs of the patient who died are interesting, inasmuch as the clinical picture was one of lobar pneumonia, while in fact it was pathologically of a pseudo-lobar type.

Leichtenstern differentiates the lesion in epidemic pneumonia from the croupous type by the fact that there is slow infiltration of part of a lobe which gradually becomes lobar in character. Flaccid heptization and a rapid transition to gray hepatization have also been noted. Aufrecht, in describing the pathology of epidemic pneumonia, states that the condition of the lung is similar to that of the stage of engorgement in the ordinary lobar pneumonia, but that in some cases grayish areas appear in the midst of the red hepatization, occasionally with marked increase in the connective tissue.

Pneumonia in children seldom runs an atypical course, and the symptoms and picture above described are not unusual in lobar pneumonia. Again the pathological picture is not marked enough to justify a separate classification.

The opinions concerning the contagiousness of epidemic pneumonia are interesting:

Aufrecht states that the disease is not inferior to erysipelas and measles in contagiousness.

Sinigar says there is no evidence of direct contagion.

Pratt believes it is contagious to a limited extent.

Preble states that there are absolutely so many instances, that if it were contagious, such cases would be of daily occurrence. To speak of contagion in connection with an organism so ubiquitous as the pneumococcus is unnecessary. He advises against isolation but that the excreta be destroyed.

Banks concludes that the communicability of pneumonia is so well established that it warrants all the sanitary restrictions which have been placed on tuberculosis.

Probably the number of epidemics of pneumonia which have been reported has given the condition an undue prominence as a distinct entity which it should not have, for careful analysis shows that the majority of cases represent merely the intensification of some of the variations of ordinary pneumonia. No special ætiological factors have been found to account for this apparent contagiousness in some attacks of pneumonia, nor were any such factors evident in this group of cases.

Summary.

(1) Out of a family of ten members, parents and eight children, one of whom lived away from home, six members developed acute pneumonia within a period of ten days.

(2) A seventh, a child of five years, developed an illness characterized by headache, stomachache, and fever several days after the onset of illness of patient VI. A week later

when seen the patient had recovered and no signs were evident in the lungs.

(3) An eighth, the father, had been ill with a "cold," hoarseness and abdominal pain for three days before the onset of illness in patient I.

(4) Two members of the family only escaped; the mother, and the daughter who lived away from home, but returned to nurse the patients.

(5) Five patients treated in the hospital proved to have uncomplicated acute pneumonia, and a sixth examined at home was found to have resolving pneumonia.

(6) One case in a girl of 14 was fatal. Pneumococci were obtained on culture from the circulating blood during life, and later at autopsy in the heart's blood. Necropsy showed a cropous pneumonia of a pseudo-lobar type.

(7) Study of the conditions under which the patients lived revealed no special ætiological factors beyond crowding and ill ventilation.

(8) It is interesting to note that where two of the patients slept together the second infection followed the first in every instance in from six to nine days.

I have to thank Dr. W. S. Thayer for the privilege of reporting these cases and for various suggestions.

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DISPLACEMENT OF THE HEART BY PLEURAL PRESSURES.

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A discussion of the mechanics of the displacement of the heart by intrapleural pressures is not of immediate practical value, yet a solution of the question must add to the knowledge of intrathoracic mechanics which, subsequently, may be of practical importance.

This article is based on one case of right-sided pleurisy with effusion, one case of double pleural effusion in a new-born, one case of cardiac displacement due to a large peritoneal abscess, and some of the principles developed in a study of pericarditis with effusion (1). The material was fixed in formalin and studied as previously described (1). Again, I am indebted to Dr. C. M. Jackson for the use of the material.

Case I. *Heart displacement.*—Is that of an old colored man, 102 years old, showing a large right pleural effusion. The displacement of the right pericardial wall and the resulting change in the right auricle are well shown. The position of the attachment of the right wall of the pericardium (*P*) to the diaphragm has not been changed. From this point the wall passes upward toward the median line, and reaches the edge of the sternum at the lower border of the third rib. Here, it comes in contact with the right wall of the ascending portion of the arch of the aorta (*C*) which it follows to its attachment to the aorta. The right auricle is compressed to occupy the angle formed by the right wall of the pericardium and diaphragm. The right ventricle is not shown. The left auricle (*G*) is distended and the left ventricle (*H*) is dilated. The remaining structures can easily be seen. (Fig. 1.)

Case II. *Double pleurisy with effusion in a new-born.*—Probably a still-born, history unknown. Weight of child, 3882 grams; length, 54 cm. The child was full term, so the displacement of the organs is due to the mechanical effects of the effusion. Points of interest in this connection only are cited. The central tendon of the diaphragm is about in normal position, it may be slightly displaced (Fig. 2). The two pleural cavities are filled with coagulated effusion, dimly shown in Fig. 2. The lungs are collapsed. The heart is collapsed, completely. Only the left ventricle contained a small amount of clear fluid. Both walls of the pericardium pass from the diaphragm almost perpendicularly upward and are closely placed against the heart. Here the heart has been caught between two pressures, in both pleural cavities, and compressed until no blood could enter the heart, when death occurred. This heart is affected similarly to that described in Case I—of pericarditis with effusion—the same mechanical factors are involved, but differently applied. The heart is not rotated as shown by the relative position of the aortic to the pulmonic valve. The vessels are normal, no malformations.

Case III. *Peritoneal abscess with upward displacement of the heart.*—Case III is that of an adult with a large peritoneal abscess which has pushed the heart directly upward, compressing it against the structures above the pericardium. All of its chambers are smaller than normal and the aorta at its junction with the heart is kinked. In a lateral direction the apex is not displaced. The lower portion of the pericardium is collapsed. No fluid in pericardium. (Figs. 3 and 4.)

The following points are of importance:

1. *The pericardium and diaphragm.* The diaphragm is attached to the base of the xyphoid process, and to the vertebral column through the crura. Its central tendon is supported by the ligamenta suspensoria diaphragmatis, first mentioned by Birand (1862) (cf. Hasse (2)) and later more fully described by Teutleben (1877) (cf. Hasse (2)). This ligament arises from the lower four cervical and upper three dorsal vertebræ, passes downward and forward to end about the large vessels and bronchi in the pericardial wall at the base of the lung. The lower portion of the ligament is formed by connective-tissue fibers of the diaphragm passing upward in the right wall of the pericardium to the base of the lung. Through this ligament the central tendon of the diaphgram and the pericardium are firmly supported from the vertebral column. Luschka says—the pericardial ligaments are strong and will support a number of pounds. The downward motion of the central tendon of the diaphragm is limited, Hasse (2) says, to 0.7 cm.; Grönroos (3), 2½ cm. Its upward motion is not so limited and must depend on the relationship between the abdominal and thoracic pressures. The pulmonary vessels, aorta near its origin, and superior cava must partake of the lateral movement of this ligament and the right wall of the pericardium. Consequently the base of the heart must be displaced an equal distance. The displaced ligament, in the right wall of the pericardium, is in a curved line between the two points of attachment.

For convenience, a right and left wall of the pericardium may be described. The right wall is composed of the ligamenta suspensoria diaphragmatis and the pericardium proper, is shorter than the left wall, and passes almost perpendicularly upward from the diaphragm. It projects only slightly into the right pleural cavity. The parietal pleura is reflected on to the pericardium near the median line in front. The left wall passes from the large vessels around the heart to connect with the diaphragm to the left of the median line. It is therefore longer than the right. The parietal pleura, in front, is reflected on to the pericardium near the median line and is between the anterior thoracic wall and the pericardium for quite a distance; it also passes under and behind the heart, so that a greater portion of the heart is covered by the left wall and a corresponding surface exposed to pressure changes in the left pleural cavity. Granting the two walls are of equal strength, through equal distances the left, being longer, is more easily displaced than the right.

In Cases I and II the central tendon is not materially depressed. This is due to the support of the ligamenta suspensoria diaphragmatis and to the fact that only a small factor of the pleural pressure is exerted in a perpendicular direction against the central tendon. This may be seen in Figs. 1 and 2.

2. *Heart.*—The heart swings free from the large vessels above and from the inferior cava below. The latter is short and firmly attached to the diaphragm, permitting perhaps

less motion than occurs in the large vessels above. The lateral movement of the large vessels with the mediastinal tissues rotates the heart through a small arc of a circle, the center of which is at the juncture of the diaphragm with the inferior cava.

The heart is a hollow, soft-walled organ, the size of which must depend on the actual amount of blood contained therein, on the intracardiac and the intrathoracic pressures. With a free flow of blood to the heart the size of the heart must depend on the relationship between the intracardiac and intrathoracic pressure, if the latter is greater the heart must be compressed, or hypodistended, as compared to a normal distension or dilatation.

The amount of blood in the heart depends on the amount delivered to the right auricle by the systemic veins.

3. *Pleural pressure.*—Aron (4) found the average normal intrapleural pressure in 36 cases to be, in inspiration minus 4.64 mm. HG, expiration minus 3.02. Regarding the changes in this pressure due to effusions, etc., much difference of opinion is expressed. Traube and Garré (cf. Holbauer (5)) say: "In pneumothorax the negative pleural pressure is relieved (or the pulling force is lost) allowing the negative pressure of the sound side to pull the organs to that side." More recently Hofbauer (5) has advocated the same idea. But if the negative pressure on the affected side is relieved the pressure of that side must be increased, so must help to push the organs to the sound side. Bard (6) says: "A normal or positive pressure is rapidly fatal and that the effect of the fluid is independent of the pressure." On the other hand most writers think a positive pressure is developed by effusions and pneumothorax, etc. Emerson (7) found in pneumothorax a pressure of 9 mm. Pitres (8) found in effusions of 1000 cc. a pressure of 8 to 20 mm. HG; 2000 cc., 20 to 44 mm. It may safely be said that in pleural effusions the intrapleural pressure is above the normal.

4. *Venous and arterial pressures.*—Recently, Gerhardt (9) has measured the venous and arterial pressure after injecting varying quantities of fluid into the pleural cavity. His results are tabulated on page 207; and show that as the quantity of fluid in the pleural cavity increases the intrapleural pressure increases; as the pleural pressure increases the pressure in the jugular vein increases and is always above that in the pleural cavity; for a time the arterial pressure is not changed, but as the pleural pressure increases the arterial pressure decreases. Under certain conditions the arterial pressure may be increased.

In Fig. 5 *A* and *B* represent two movable walls, separated by a flexible bag *C* to which is attached a tube *D*, this bag is filled with fluid.

If *A* is pushed toward *B*, *C* is collapsed, when there is no pressure in *C*. But if the pressure in *C* is greater than the pressure necessary to move *B*, *C* fails to collapse, and the pressure exerted by the movement of *A* is transferred through *C* to *B* which must be moved a distance equal to the distance *A* moves. If there is a certain amount of pressure in *C*, say less than is necessary to move *B* and the tube *D* is closed, the movement of *A* toward *B* will compress *C* until the pressure in *C* is equal to that necessary to move *B*, then *B* is displaced, preventing a further rise of pressure in *C*. Consequently the displacement of *B* by the movement of *A* depends on the relationship of the pressure in *C* to the resistance offered by *B*; if pressure in *C* is less than the resistance of *B*, *B* will not be displaced, if equal to or greater, *B* will be displaced until the increased tension of *B* equals the pressure in *C*. Beyond this point *C* will be collapsed by further movement of *A* unless the pressure in *C* is further increased. Or the greater the displacement of *B* the greater must be the pressure in *C*. The pressure in *C* must have a limit when further movement of *A* will collapse *C* and not cause further displacement of *B*. Or as *A* moves toward *B*, *C* must compensate the pressure exerted by *A* to keep from collapse, or as *A* moves toward *B* the pressure in *C* must increase and further displace *B*.

Transfer Fig. 5 to the thorax and let *A* represent the left wall of the pericardium; *B*, right wall; *C*, the heart; *D*, the venæ cavæ. The flexible, elastic pericardial wall surrounds the heart. A pressure exerted against the left wall must press it against the heart and transfer the pressure directly to the heart. The heart is displaced until it encounters the resistance of the right wall. As soon as this resistance is developed the normal relationship of the auricular and pleural pressure are disturbed (pleural increased). Consequently the heart is compressed until the pressures are relatively normal after which the heart maintains its size and transmits the entire pleural pressure to the right wall of the pericardium. While this readjustment of auricular pressure is taking place, a portion of the pleural pressure is used to force blood from the heart backward into the veins, or what amounts to the same thing, prevents blood from flowing to the heart. Or a venous congestion and rise of pressure develops to compensate the heart against the pleural pressure and to prevent a collapse of the heart between the two pericardial walls, as shown in Case II. The right wall of the pericardium is displaced by the pleural pressure exerted through the heart.

So long as venous compensation continues the heart maintains its normal size. Room for the heart is made by the displacement of the opposite pericardial wall. But a time comes when to further displace the pericardial wall requires more pressure than can be delivered to the heart. From this time the heart begins to diminish in size, due to the venous pressure failing to compensate. The heart is hypodistended, and displaced in the pericardium which is collapsed as shown in Case III.

In addition to the above general consideration, differences in the effect of pleural pressures in the two sides may be noted.

Effusion on the Right Side.—Displacement of the heart to the left on change of position may be as much as 6 cm., more commonly 4 cm., without undue stretching of the left wall of the pericardium.

Two simultaneous effects are produced by the effusion: First, on the right side the venæ cavæ are directly exposed to the pleural pressure which must compress them, causing a congestion and rise in pressure. This rise in pressure compen-

sates the pleural pressure and delivers blood to the right auricle under an increased pressure and in larger than normal quantities. Second, the right wall of the pericardium is displaced to the left pushing the heart before it, to take up the 3 or 4 cm. of possible (passive) displacement of the heart. Beyond this point the left wall resists further displacement of the heart and thereby changes the normal relationship of the auricular and pleural pressure. These two factors produce an increased amount of blood delivered to the heart under an increased pressure without a corresponding increase in the auricular pressure. This results in (1) an increased rate of pulsation, (2) increased quantity of blood in the heart or a dilatation, and (3) an increased output of blood which results in an increased arterial tension. Hensen (10) records a relatively high tension in a right-sided pleurisy.

The displacement to the left must depend on the degree of pressure in the right pleural cavity, the resistance offered by the left wall, and the degree of distension of the heart. If the left wall is too weak to resist the pleural pressure, the right wall must support all of it. In this event changes in the auricular pressure are caused, mainly, by the changes in the venous circulation. In all cases the right wall supports a portion of the pressure. So long as venous compensation is maintained the heart must remain normal in size or slightly dilated, but when the pleural pressure begins to diminish the flow of blood to the heart, the heart must become smaller with a proportionally diminished displacement, and a decrease in arterial pressure.

Left-sided Pleurisy.—The left pleural cavity passes in front of, under, and behind the heart, consequently the pleural pressure is directed against a large portion of the surface of the heart. The left auricle is directly exposed to the pleural pressure, consequently must be compressed until the auricular pressure regains its normal relationship to the pleural. This change in the auricular pressure is compensated by the right ventricle. While the above has been taking place the heart as a whole has been pushed to the right against the right wall of the pericardium, compressing the right auricle and obstructing the venous circulation as described.

Two mechanisms for compensating the pleural pressure are necessary, the right ventricle for the left auricle, and the venous congestion for the right auricle. Either or both of these mechanisms may fail. If the venous compensation is competent and the right ventricle fails, the right ventricle must dilate to receive the blood forced into it by the auricle and the left heart must be proportionally smaller. If the venous compensation fails sufficient blood is not delivered to the heart, which becomes smaller or is collapsed as shown in Case II. If both mechanisms remain competent, the pleural pressure increases and further displaces the right wall until it requires more pressure to displace the wall than it does to compress the heart. Now the heart becomes smaller, as shown in Cases II and III, the apex approaches the base and also the sternum. The degree of displacement of the apex is determined by elasticity of the right wall of the pericardium and the degree of distension of the heart. The displacement of the apex from the left side may, in part, be due to the fluid coming in between the anterior wall and the pericardium. As the apex moves to the right the auricles are further compressed to permit the heart to swing about the large vessels (as a door on its hinges). The aorta and pulmonic arteries are carried slightly to the right, causing a slight rotation of the heart from left to right, due to fixation of the heart by the inferior cava. When the pressure within the left ventricle and aorta become less than the resistance of the mediastinal tissues the aorta must be kinked. This point is shown in Case III, but has not been pictured.

The reputed downward displacement of the diaphragm by the apex in its movement to the right can be determined by direct observation only. Considering all the factors involved, it would appear impossible. The power of the heart to displace the diaphragm is equal to the intracardiac pressure. This pressure is exerted near the attachment of the diaphragm to the anterior thoracic wall. Here, it seems, more pressure would be required to displace the diaphragm than nearer the center, where in two cases it is displaced only slightly, if at all.

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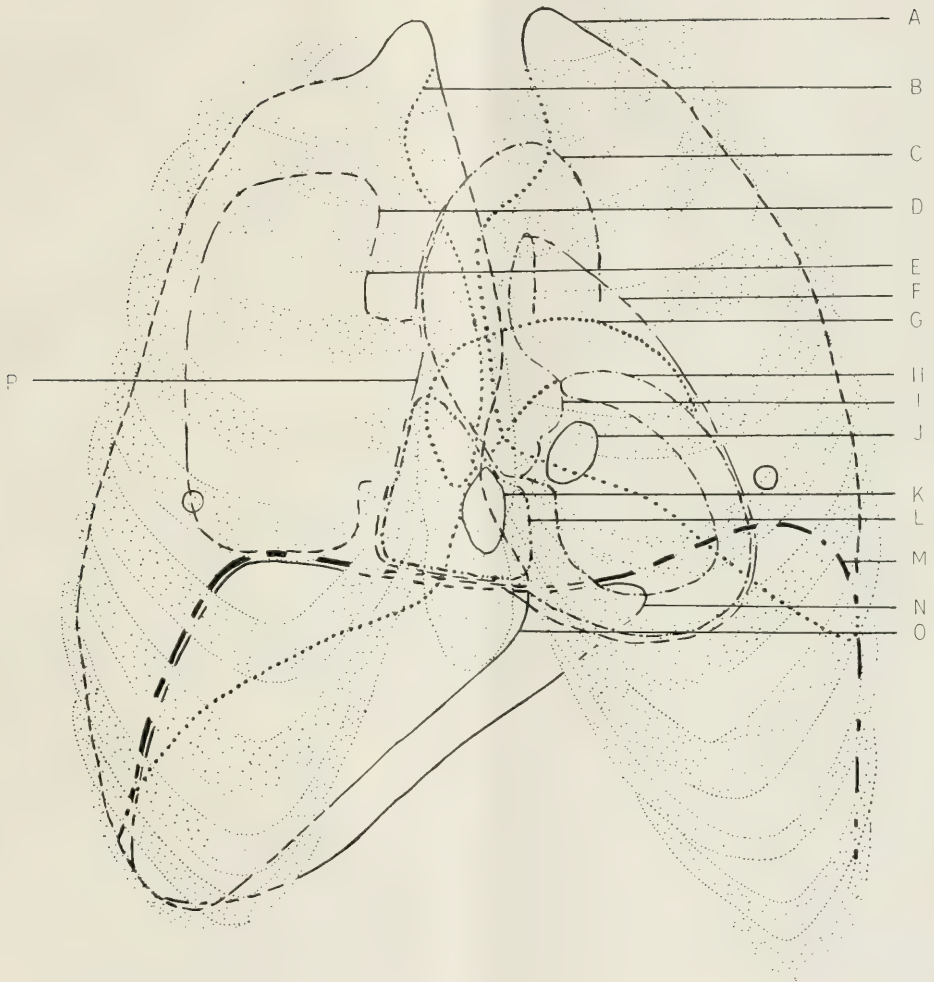

FIG. 1.—*A*, boundary of left pleural cavity; in the front portion of the body it is shown in large dots; *B*, anterior border of right pleural cavity, also shown in large dots; *C*, arch of aorta; *D*, right lung collapsed; *F*, pericardium; *G*, left auricle; *H*, left ventricle; *I*, aortic valve; *J*, mitral opening; *K*, tricuspid opening; *L*, right auricle; *M*, diaphragm; *N*, liver; *O*, posterior boundary of right pleural cavity; *P*, right wall of pericardium.

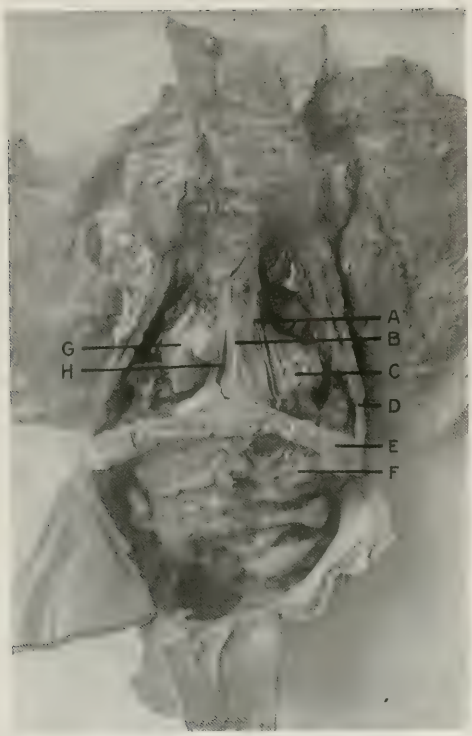

FIG. 2.—New-born. Double pleurisy with effusion, ascites. *A*, the left, *H*, the right wall of the pericardium; *B*, collapsed heart; *C*, remains of left lung; *D*, thoracic wall; *E*, that portion of the thoracic wall to which the diaphragm is attached; *F*, liver; *G*, middle lobe of the right lung.

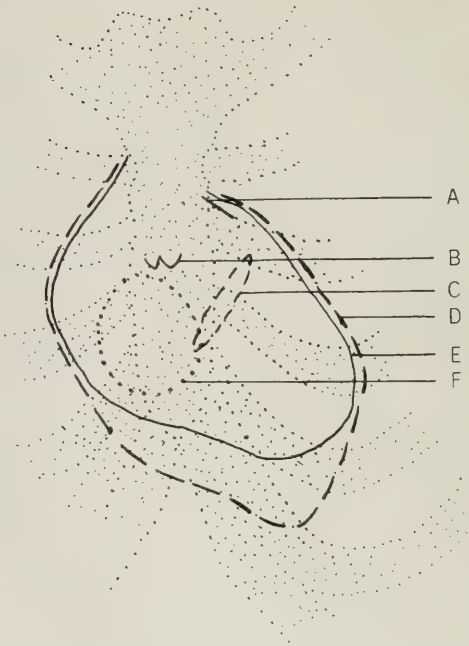

FIG. 3.—Front projection, showing the outline of the heart and pericardium. *A*, pulmonic valve; *B*, aortic valve; *C*, mitral; *F*, tricuspid valve; *D*, pericardium; *E*, heart.

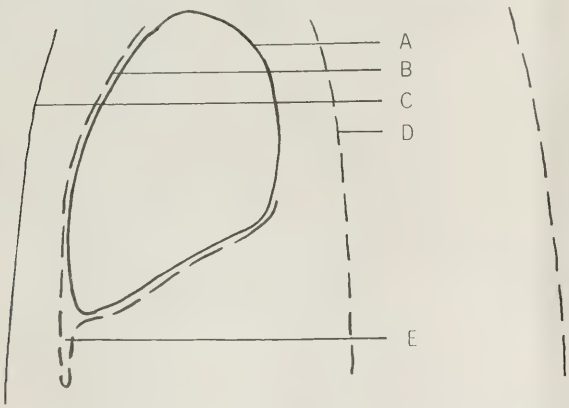

FIG. 4.—Sagittal section of Case III. *A*, heart; *B*, pericardium; *C*, anterior thoracic wall; *D*, anterior border of vertebral column; *E*, collapsed portion of the pericardium.

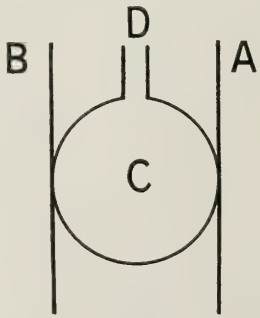

FIG. 5.

COMPENSATORY VENOUS CONGESTION.

By W. J. Calvert, M. D.,

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In discussing compensation of tricuspid insufficiency, Franke (1), after giving a brief historical statement, reviews the work of Stadler, and calls attention to the rôle of congestion of the venæ cavæ and its branches, especially those of the liver. In one of his cases, he noted the absence of the præsystolic venous pulsation due to the systole of the auricle, from which he concludes that in this case the auricle was passive, so took no part in compensation. Three factors in tricuspid compensation are given: (a) Activity of right ventricle; (b) elasticity and passive resistance of the venous system and right auricle, and (c) the activity of the peripheral circulation, etc., especially the liver. In conclusion Franke says: "When the compensation of the mitral and tricuspid insufficiency are compared, it is seen that the liver and peripheral vessels play the same rôle in compensation of the tricuspid valve as the right ventricle plays in compensating mitral insufficiency."

In experimental tricuspid insufficiency in dogs, Stadler (2) found hypertrophy and dilatation of the right ventricle and auricle, normal or atrophied left ventricle, general venous congestion, and in some cases subcutaneous œdema.

Salaman (3) found that a normal liver under high pressure holds its volume of water, most of which is expelled when the pressure is removed. He likens the liver to a sponge. Continued pressure destroys this elasticity and interferes with the degree of activity of the liver in compensating heart lesions in the order of the pathological changes produced, as follows:

1. Engorged liver—perfectly compensated heart lesion.

2. Nutmeg liver—prolonged back pressure—with some fatty changes and cirrhosis in the center of the lobule.

3. Cirrhotic nutmeg liver—portal, hepatic, and central fibrosis are well marked—liver is small, hard and due to long standing back pressure.

In the above discussions the activity of the heart complicates, by introducing too many factors, the general question of the rôle of venous system and the liver as factors in compensating the tricuspid valve. Consequently, if the heart can be eliminated the rôle of venous congestion can be more easily discussed, and its importance more clearly shown. In pericarditis with effusion the heart can be eliminated, for the pressure of the pericardial fluid acts on that portion of the venæ cavæ within the pericardium, consequently affects the venous circulation before the blood reaches the heart and before the heart can possibly have any effect on the venous congestion. Two cases of pericarditis have been studied. In one that portion of the venæ cavæ within the pericardium was collapsed; in the second, dilated, as illustrated (4).

This observation shows that when the pericardial pressure is sufficiently high the venæ cavæ within the sac are collapsed and when low the veins are open. Some pressure must keep them open. The only pressure at hand is the venous pressure due to the congestion. The venous congestion then must compensate the pressure of the pericardial fluid on the venæ cavæ within the pericardium. This compensation must continue, unaided, until the limit of venous pressure is reached, after which an additional rise in pericardial pressure must collapse the veins within the pericardium, thereby preventing the flow of blood to the heart. As the maximum venous pressure can be produced in pericarditis with effusion, no greater pressure can be caused by tricuspid lesions. As the venous pressure, unaided, can compensate pericardial pressures, it must follow that to the same degree it can compensate tricuspid lesions. Here the activity of the right auricle must be taken into account. But, if inactive, as suggested by Franke, the auricle is dilated and simply adds that much blood to the venous congestion.

The venous congestion, including the liver and right auricle, in tricuspid insufficiency must be likened to the left auricle, pulmonic congestion and right ventricle in mitral insufficiency. While the right ventricle in tricuspid lesions plays the same rôle as the left ventricle, in mitral lesions.

On account of the importance of venous congestion in compensating pericardial (5) and pleural (6) effusions, pneumothorax and tricuspid lesions, the name "compensatory venous congestion" is proposed as a term which more accurately describes the function of the congestion than the term "chronic passive congestion" which was adapted at a time when the rôle of the congestion had, probably, not been fully considered.

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ECLAMPSIA WITHOUT CONVULSIONS.

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The disease which is now universally designated as eclampsia was described by the earliest medical authors, but its present apellation dates from comparatively modern times. The word itself derived from the Greek εκ, forth, and λαμπειν, to shine, was used in classical literature to describe a flash of lightning or the sudden beaming of the sun through the clouds. When first introduced into medical terminology the word eclampsia was not used in connection with the disease with which it is now associated, but was employed to denote a sudden rise in temperature. It was used in this sense by Hippocrates and throughout the Middle Ages.

According to Knapp and Kossman, the first instance in which the term was applied to convulsive seizures occurs in The Nosology of Boissier von Sauvage, published in 1760. Under the caption Eclampsia, the latter classified all non-periodic fits other than epileptic, but made a separate group of the convulsions occuring during pregnancy, which were designated as "Eclampsia parturientium." Gehler, a professor of physiology in Leipzig, adopted this term and made use of it in theses written in 1776 and 1777. For some time the use of the term remained purely local, but it gradually gained favor, so that fifty years later its use had become current throughout the continent.

The convulsive attacks, which finally gave the disease its enduring name, have always been its most prominent clinical feature, and this they remain. However, it is of prime importance to recognize that they are not the disease itself, but merely constitute one of its symptoms. Disregard of this fact leads to the diagnosis of eclampsia in all conditions in which convulsions occur during pregnancy. Should the pathologist accept without question such clinical diagnoses, his findings at autopsy would vary so greatly that it would be impossible to regard any lesion as specific; whereas, in truth, the pathological anatomy of eclampsia is most characteristic and offers the only means by which an unimpeachable diagnosis can be made.

Since the appearance of Schmorl's monograph in 1893, it has been generally conceded that the typical anatomical findings in eclampsia consist of degenerative changes in the kidney and myocardium, hæmorrhages into the brain and focal necroses in the liver. The last constitute the most important eclamptic lesion and would seem to be areas of infarction dependent upon thrombosis of the smaller portal vessels. The areas of necrosis may be either hæmorrhagic or anæmic in character, but always maintain a regular topographical disposition, appearing first in the portal spaces and invading the peripheral zone of the lobule. Schmorl's observations have been abundantly substantiated by Jürgens, Klebs, Pilliet, Bouffe de Saint Blaise, Prutz, Lubarsch, Pels Leusden, Bar, Williams, Jung, Chiari, Sandberg, and Lindfors and many others.

The changes in the liver are most characteristic, and Schmorl regards them as absolutely pathognomonic, having noted them in 70 out of 72 cases, and in the two negative instances there was total thrombosis of the portal vein. In a recent study of the liver in 500 autopsies at the Johns Hopkins Hospital, Opie noted such lesions only in eclampsia; while Williams has met with them so regularly at autopsy upon eclamptics that he considers that their presence justifies the diagnosis of the disease, even in the absence of a clinical history.

Unfortunately, we are not in possession of any clinical phenomenon in eclampsia which may be fairly said to point to the occurrence of this specific change in the liver. All the signs and symptoms, as we know them now, may occur in a number of other conditions. Thus, Lloyd has lately recorded an instance of uræmia during pregnancy in which the clinical picture was identical with that obtaining in typical eclampsia, yet the autopsy revealed a profound acute necrosis of both kidneys without any change in the other viscera. Likewise, acute yellow atrophy of the liver may be indistinguishable from eclampsia at the bedside, while occasionally it may be impossible to make a differential diagnosis between it and epilepsy or even hysteria.

Again the obstetrician should bear in mind the fact that the toxic action of certain drugs may simulate eclampsia, particularly as women who are illegitimately pregnant may take poison with suicidal intent. Knapp has met with cases of strychnine poisoning and Schild with intoxication from nitro-benzol which could not be distinguished from eclampsia by the symptomatology. Lead, phosphorus, carbolic acid, corrosive sublimate and mushroom poisoning also give rise to toxic manifestations which may be characterized by convulsions and coma.

The difficulty in making a positive clinical diagnosis of eclampsia is still further increased by the fact that the disease sometimes appears in an atypical form. Thus, the customary convulsive attacks, the very symptom which has given the disease its name, may be absent throughout its course. Two such cases have come under observation in the Obstetrical Department of the Johns Hopkins Hospital, and I am indebted to Dr. Williams for the opportunity of making this report. The diagnosis in each instance was obscure, until the characteristic hepatic changes were demonstrated at autopsy; and in view of their presence, it was evident that both cases were examples of the somewhat paradoxical condition—eclampsia without convulsions.

CASE I.—Obstetrical No. 909. K. B., negro, IV p., aged 27.

The patient applied for registration in the out-patient department April 25, 1901. She stated that her four previous pregnancies had been normal. Her labors and convalescence had always been free from any complication. During the present pregnancy she has been quite well.

May 2. She visited the dispensary to bring a specimen of urine previously requested. This showed 0.05 gm. of albumin to the liter, but contained no casts. There were no subjective symptoms.

June 4. She complained of swelling of the feet and legs, but had no headache, visual disturbance or other subjective symptoms. The urine presented a large amount of albumin without casts. She was advised to enter the hospital, but declined.

June 12. Delivered by the Out-patient Service at 10.30 p. m., after a normal labor of 18 hours. Child was a male, 50 cm. in length, and weighed 7¼ pounds. The mother's condition was good when left at midnight.

June 13. When the nurse called at 9 a. m. to pay her daily visit, she found the woman in a semi-conscious condition, with a normal temperature and a pulse of 46 to the minute. The family stated that no convulsion had occurred, and attached little importance to the drowsy condition of the patient, but after considerable delay, reluctantly consented to have her removed to the hospital.

Examination on admission to the hospital two hours later. The patient is a stout colored woman presenting marked œdema, especially of face, hands, and feet. She is semi-conscious and arouses slightly when questioned, yet cannot be made to answer. The breathing is stertorous. Pupils contracted. Temperature, 98.4°. Pulse, 64. Heart sounds clear. There are definite signs of fluid in both pleural cavities and in the abdomen. The urine, 520 cc. by catheter, is neutral in reaction and has a specific gravity of 1010. The albuminous precipitation is heavy. On microscopical examination, casts of varied type and red blood cells are found. Soon after entering the hospital 400 cc. of blood were taken from one of the veins of the arm and an equal amount of normal saline solution transfused. Following this a sweat bath was given. The patient did not respond; gradually became profoundly comatose and died, without having had a convulsion, at 4.45 p. m. the same day.

Autopsy (Path. No. 1749).—Permission was obtained for a post-mortem examination with great difficulty, so that it could not be made until the day after death. As an agonal infection with the gas bacillus had occurred, all the tissues and organs of the body presented an emphysematous appearance, which in a measure marred the anatomical findings. The autopsy was performed by Dr. W. G. MacCallum, who kindly placed the following notes at my disposal.

Anatomical diagnosis.—Puerperal uterus. Hydronephrosis and hydro-ureter. Chronic nephritis with hæmorrhage. Hæmorrhages into liver. Acute spleen tumor. Œdema of lungs. Distension of veins with gas. Emphysematous organs. Interstitial emphysema of lungs.

Body of a stoutly built negro woman, 165 cm. long. The abdomen is distended, and on being opened is found to contain blood-stained fluid. The peritoneal surfaces are smooth everywhere.

Both pleural cavities as well as the pericardial cavity contain bloody fluid.

Heart weighs 340 gm. Endocardium smooth. Valves are normal.

Both lungs present a smooth surface. No areas of consolidation are found.

Spleen weighs 230 gm. No macroscopic lesion noted.

Liver measures 25 x 18 x 9½ cm. Over almost the whole surface of the right lobe an extensive subserous hæmorrhage is seen. Smaller hæmorrhages are scattered over the remaining surface of the organ. On section, the lobules are extremely pale and opaque. The greater part of the right lobe shows conglomerate hæmorrhages throughout its substance. These obscure the lobulations. Small gray points can be seen among the fresh hæmorrhages and here the consistence is much firmer. These are evidently areas of liver tissue. Other hæmorrhages occur throughout the liver.

Kidneys. Left: Capsule strips off easily. On section, one notes hæmorrhages into the substance of the organ. The pelvis of the kidney as well as the ureter is distended. Right: Somewhat larger than left, but presents the same general appearance. The ureter is slightly distended, but much less so than on left side. No obstruction, other than the uterus, can be found blocking the ureters.

Stomach is distended with gas, but otherwise is normal.

Pancreas is emphysematous, but otherwise normal.

Brain: On opening the skull, no puerperal osteophytes are found.

The cortex is normal in appearance, except for an atrophic area behind the fissure of Rolando on the left side. (No notes were made as to the quantity of cerebro-spinal fluid. The condition of the brain substance or the condition of the lateral ventricles.)

The uterus rises 16 cm. above symphysis. Its surface is smooth and glistening.

Microscopical examination.—Liver: A large portion of the organ is made up of necrotic tissue in which the nuclei are indistinct or totally missing. The cell protoplasm stains deeply with eosin. Between the dead cells there is an extensive infiltration with blood.

Other sections show the liver cells in a better state of preservation as a whole, but numerous foci of degeneration and necrosis are noted. The fresher ones are accurately confined to the portal spaces with the bile duct approximately in their centers, while the adjacent blood vessels are thrombosed. A few of these areas are anæmic, but for the most part they are infiltrated by hæmorrhage.

Larger areas of necrosis predominate, involving all or parts of several lobules. They appear to have resulted from the fusion of smaller areas of infarction, or from a secondary extension from a single portal space. Practically everywhere the liver is infiltrated with blood.

Kidney: A general increase in connective tissue is apparent throughout the section.

The cells of the straight and particularly of the convoluted tubules are the seat of marked degeneration. The cell nuclei having disappeared, the cytoplasm is converted into hyaline material. Some of the glomeruli are contracted, and lie in what are apparently retention cysts. In other places they are swollen and completely fill the surrounding capsule.

Spleen: Pulp is engorged with blood. The vessels in the center of the Malpighian corpuscles contain thrombi and are surrounded by masses of hyaline material, frequently occupying half of the tuft. Under the high power these are seen to be made up of areas of agglutinated red blood corpuscles.

Heart: The myocardium presents a mild parenchymatous degeneration.

Lung: Blood vessels distended. Alveoli show œdematous changes, but do not contain any inflammatory exudate.

CASE II.—Obstetric No. 1722, L. C., white, primigravida, aged 33.

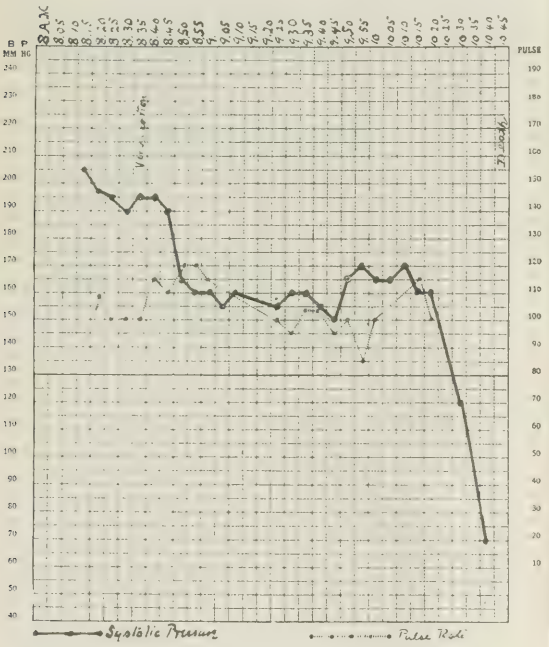
The history prior to admission was obtained from the patient's mother, an intelligent woman, whose statements gave the impression of accuracy and trustworthiness.

The patient has always been rather delicate. As a child she had diphtheritic croup and measles. Both these attacked her with more than ordinary severity. No other serious illness can be remembered. She frequently had "spells," which were usually associated with the mentsrual period, and in which she suffered from nausea, vomiting, headache, swelling of the feet and legs, and puffiness about the face.

The last menstruation occurred in August, 1903. Since then she has never felt well and has complained of a good deal of headache and difficulty in reading, on account of "seeing double." She is habitually constipated. Her whole body has been swollen for some weeks. The patient has never mentioned passing less urine than usual, nor any other peculiarity of micturition. A decided change for the worse in her condition occurred about the middle of February, when she "caught cold." Since then the headache has been more severe and the swelling has increased.

Two weeks ago the patient was threatened with premature labor, and had considrable bleeding, which ceased after a few days. She did not have abdominal pain on this occasion, or at any other time. The day before admission she was more uncomfortable than usual, but was not sick enough to go to bed. After retiring at the customary hour, she awakened her mother about 3 a. m., when she complained of "sick stomach" and was violently nauseated for half an hour, but did not vomit. Immediately afterwards she fell into a stupor and did not regain consciousness. The patient's husband, mother and father, who came to the hospital with her, all agreed in the statement that she had not had a convulsion of any kind.

Examination on admission.—March 12, 1904, 7.15 a. m. Patient is a stout woman, weighing about 200 pounds. She is in profound coma and all attempts to arouse her fail to elicit the slightest response. Face is cyanotic and swollen. Pupils are contracted. Conjunctival reflex is absent. Lips are quite blue and do not present any abrasion. Tongue is uninjured. There is a sweetish odor to the breath. Lungs are negative on percussion and auscultation. Respirations 20 to minute, are alternately shallow and deep, closely resembling the Cheyne-Stokes' type. Heart sounds are clear at apex and base. Pulse is full, of high tension, regular in force and rhythm. Systematic observations as to its rate and the systolic blood pressure (Riva Rocci apparatus) are given in the accompanying chart.



Abdomen is distended by the pregnant uterus which rises three fingers breadth above the umbilicus. There is dullness in both flanks. Feet and legs are markedly swollen and readily pit on slight pressure. Temperature by rectum is 99.2°. Vaginal touch shows the cervix long and snout-like. The external os is intact. The cervical canal is approximately 3 cm. in length.

Urinalysis.—Two hundred cubic centimeters of amber colored urine were obtained by catheterization. Microscopical examination showed an unusually large number of hyaline and granular casts, with many red blood cells and a few leucocytes.

The chemical analysis of the specimen was as follows: Reaction, acid; specific gravity, 1025; no sugar. Total nitrogen (Kjeldahl) = 2.66 grams; albumen (Esbach) = 2.5% (25 grams per liter); therefore, the non-albuminous nitrogen = 1.91 grams. Ammonia (Schlössing) = .16 gm. = 6.8%.

Nitrogen division.—Nitrogen precipitated by phosphotungstic acid = 1.31 grams.

Therefore,

Non-albuminous precipitate — N. = .564 gm. = 29.5%
Urea — N. = 1.189 " = 62.2%
Amido acid — N. = .141 " = 7.3%

Treatment.—The patient was so ill on admission that an *accouchement forcé* was inadvisable. Induction of labor by a slow method with the simultaneous use of medicinal measures was thought to offer the only possible means of relieving her condition, though little if any hope was entertained of her recovery.

After stretching the internal os with a Goodell dilator until it had a diameter of 1 to 2 cm., a small rubber balloon was introduced into the uterus and inflated with normal salt solution, after which the cervix and vagina were packed with sterile gauze. Anæsthesia was not necessary during these precautions.

A vein was opened in the forearm and 500 cc. of blood allowed to escape, which was immediately replaced by a similar amount of 1% sodium bicarbonate solution given subcutaneously. A quantity of bile-stained fluid was washed out by gastric lavage, after which two ounces of Epsom salts and one drachm of sodium bicarbonate were left in the stomach. The patient was given a sweat bath at 9 a. m., but did not respond satisfactorily. Her condition gradually grew worse and she died at 10.45 a. m.

During the three and a half hours from the time of admission to the hospital until death she had no convulsions and was continually in profound coma.

Autopsy (Path. No. 2265) was performed four hours after death by Dr. W. G. MacCallum, whose notes were as follows:

Anatomical diagnosis.—Pregnancy, 7 months; chyliform ascites; generalized œdema; basal atalectasis of lung; focal necrosis in liver; erosion of mucosa of stomach; accessory spleen

Body of a very stout woman, 172 cm. in length.

On opening the peritoneal cavity, it is found to contain about two liters of an opalescent fluid. The peritoneum is smooth and glistening.

The pleural cavity contains a little of the same kind of fluid and its surfaces are smooth. The pericardium is free from excess of fluid, but all the tissues are œdematous.

Heart is not enlarged. Foramen ovale is open. All the valves are normal. The coronary arteries are not sclerotic.

Lungs: The left lung is everywhere crepitant, except in the lower and posterior portions where it is collapsed. The right lung presents a similar appearance.

Spleen weighs 220 gms. It is somewhat enlarged, and soft and flabby, but apparently normal on section. Adjacent to it are found two small accessory spleens.

Liver weighs 1590 gms., is remarkably firm and distinctly diminished in size, measuring 21 x 18 x 8.5 cm. Under the markedly thickened capsule numerous small, irregular hæmorrhages are seen upon the surface of the upper and lower parts of the right lobe.

On section inconspicuous focal areas of alteration in the liver tissue may be seen after careful inspection. They are opaque, yellow in appearance, and would seem about the size of three lobules. In general the lobulation is everywhere quite distinct. A few very small hæmorrhages are scattered throughout the liver substance.

Kidneys: The two organs are practically alike. The capsule strips off readily, leaving a smooth, rather pale, grey surface, on which the stellate veins stand out prominently. Fœtal lobulation is quite evident. On section the cortex is found to be 5 to 6 mm. in thickness. Its striations are quite straight. The labyrinthine portion is somewhat opaque. The straight tubules stand out definitely and are translucent. The glomeruli appear as prominent greyish dots.

Stomach is normal in appearance. Just below the pylorus there is a small erosion 4 mm. in diameter. The mucous membrane of the duodenum is œdematous. Pancreas is œdematous, but otherwise normal.

Thyroid is distinctly enlarged and measures 6 cm. in length and 3.5 cm. in width. In section, an increase in connective tissue is evident, otherwise there is nothing abnormal in the right lobe. In the left lobe there is a cyst containing a brown, colloid fluid. Parathyroids are apparently normal.

Œsophagus and trachea are normal. The gall ducts are normal.

Uterus measures 25 x 20 x 13 cm. and is normal in its external appearance. Cervix practically undilated and only admits tip of little finger. Canal intact. On opening the organ, the placenta is found attached to its anterior wall, and is separated from its attachment for a distance of 3 cm. from its lower edge. Beneath the placenta there is a blood clot 1 x 2 x 2.5 cm. and other clots are found between it and the internal os, the membranes having been dissected from the uterine wall. The partial separation would readily explain the bleeding from which the patient suffered during the last two weeks of life. Fœtus is a male, measures 24 cm. from vertex to sacrum and does not present any external abnormality.

Tubes and ovaries are normal. The left ovary contains the corpus luteum of pregnancy.

Microscopical examination.—Liver: Immediately around the portal vein a varying number of liver cells are necrotic and have been converted into a mass of hyaline material through which leucocytes are scattered. Sometimes these areas are infiltrated by hæmorrhage. The centers and middle zones of the lobules present a normal appearance, save that here and there foci occur in which the liver cells are swollen and almost transparent.

Spleen: Central portions of Malpighian bodies show fragmentation of the cells with formation of a coagulum. In the splenic pulp the vessels are sharply marked out. The fibrous tissue appears to be slightly increased.

Kidney: The glomeruli are normal. Epithelium of convoluted tubules appears somewhat ragged. The tubules contain some débris. There is an inflammatory exudate in the kidney.

Thyroid: Alveoli greatly enlarged, cells lining them are well preserved as a rule, though here and there they melt into hyaline masses with irregular outline, in which the nuclei are extremely small, deeply stained and shrunken; the colloid material is sometimes seen to extend between the cells.

Lungs: In some places the lungs show complete atalectasis, but for the most part they present no other changes than those seen in pulmonary œdema.

Thymus: Considerable remains are found in the form of long strands.

Bacteriology: Cultures from the various organs and the blood are negative.

The first record of a case in which eclamptic lesions were found in the liver at autopsy without a preceding clinical history of convulsive attacks is to be found in the Paris thesis of Bouffe de Saint Blaise in 1891. His patient was suffering from a profound toxæmia of pregnancy and was delivered by *accouchement forcé*. Death occurred a few days later from peritonitis. A similar instance was reported by Wendt in 1898, where the operation was immediately followed by a fatal post-partum hæmorrhage.

These cases were of considerable importance at the time in silencing the objections of Winkler and others, who urged that the hæmorrhages in the liver and elsewhere were the result of the eclamptic seizures and therefore not pathognomonic of the disease. They are also of great interest to us now, as they indicate that the characteristic organic changes in the liver may occur in pre-eclamptic toxæmia; but at the same time they cannot be placed in the same category with the two cases which I have just reported, since there is no evidence that convulsions might not have occurred had the patients not succumbed to complications incident to the mode of delivery.

In 1902, Schmorl placed on record three cases of eclampsia without convulsions, in which death occurred in coma, and autopsy revealed characteristic lesions. Subsequently two similar cases were reported by Meyer-Wirtz and Esch, respectively. These five cases are analogous to our own and supply a basis for comparison, as well as material for an analytical study of the condition. Labhardt, in a recent communication, incidentally mentions having met with a similar instance, but fails to give any clinical or pathological data.

Clinical Course.

The incidence of this type of eclampsia bears no relation to age, as the statistics indicate that women are subject to it throughout the childbearing period. A predisposition on the part of primigravidæ, and the onset of the condition in the second half of the pregnancy is seen, but in these respects it is entirely analogous to the usual form of eclampsia. Again, there is nothing characteristic in the relation of the disease to labor. While it has been observed more frequently before parturition, it may also occur during labor and in the puerperium.

The clinical history in all the cases gives evidence of the existence of a toxæmia prior to the appearance of coma. Such manifestations, however, are extremely variable and may persist through several months or last only a few days.

Headache and albuminuria with casts were invariably noted, although in one of Schmorl's cases albumin did not appear until shortly before death. Œdema, jaundice, nausea, and vomiting may occur as premonitory signs, but not necessarily. Preliminary visual disturbances were very common and would seem to possess a particular significance. Usually the patients complained of black spots before the eyes, dimness of sight or double vision, while Esch's case became totally blind and one of Schmorl's cases showed a left oculo-motor paralysis.

Consciousness usually disappears slowly. At first the patient is drowsy and stupid, later she becomes unconscious,

and finally passes into profound coma, the gradual transition occupying several hours. Occasionally, however, the woman has passed very suddenly from normal mentality to complete coma. Thus, in Meyer-Wirtz's case, the patient complained of intense headache and nausea two hours after delivery and quickly lapsed into deep coma. The duration of the coma has varied from 5 to 11 hours, except in one of Schmorl's cases, in which it seems to have persisted for a longer time, possibly 24 hours, although its exact duration cannot be determined from the data given.

CLINICAL SUMMARY OF CASES.

No.	Reported by	Age of Pt.	Para.	Variety.	Duration of Pregnancy.	Premonitory Symptoms.	Duration of Coma.	Obstetrical Condition.	Clinical Diagnosis.	Pulse.	Temp.	Respiration.
1	Schmorl.	32	I	Ante-partum.	6 mos.	Headache, jaundice, œdema, albumen and casts.	7 hours.	Undelivered.	Uræmia.	120	37.3 C.	Dyspnœa.
2	Do.	23	III	Do.	6 mos.	Headache, double vision, vertigo, left oculo-motor paralysis, urine heavy with albumin; before death, no œdema.	Not stated.	Do.	Cerebral syphilis.	Rapid.	No note.	No note.
3	Do.	37	X	Do.	8 mos.	Headache, vomiting, sleeplessness, albuminuria with casts.	6 hours.	Do.	Uræmia.	Do.	37.3 C.	Do.
4	Meyer-Wirtz.	38	I	Post partum.	9 hrs.	Headache, cyanosis, albumin with casts.	5 hours.	Delivered spontaneously.	....(?)	96	37.5 C.	Temporary cessation.
5	Esch.	25	I	Intra partum.	10 hrs.	Headache, dim vision, vomiting, albuminuria, total loss of sight, no œdema.	11 hours.	Undelivered.	....(?).....	84	39.7 C.	Deep and stertorous.
6	Slemons.	37	IV	Post-partum.	10 hrs.	Headache, œdema, albuminuria with casts.	6 hours.	Delivered spontaneously.	....(?).....	46	98.4° F.	Stertorous.
7	Do.	33	I	Ante-partum.	7 mos.	Headache, œdema, double vision, vomiting, albuminuria with casts, premature separation of placenta.	7 hours.	Undelivered.	Uræmia.	84	99.2° F.	Periodic.

The temperature is usually normal, but finally became elevated to 102° and 104° in the cases of Meyer-Wirtz and Esch, respectively. The pulse rate is not characteristic; more frequently it is slow at the onset of the coma and later becomes rapid, ranging between 120 and 160 to the minute. The usual findings are similar to those represented in the preceding chart, which also gives the only blood pressure observations that have been made in any of the cases. Irregularities in the force or the rhythm of the pulse have received slight mention.

The character of the respiration was commented upon in five of the seven cases. Deep stertorous breathing was noted by Esch, as well as in our first case, while dyspnœa occurred in one of Schmorl's cases. Respiration ceased in Meyer-Wirtz's patient at the onset of coma, but was re-established by artificial means; while our second case exhibited most marked irregular breathing, which differed from typical Cheyne-Stokes' respiration only in that there was no period of complete apnœa.

Pathology.

The pathological findings in all these cases have conformed to the anatomical picture of eclampsia, so that there can be no doubt as to the accuracy of the diagnosis. Indeed, the only question is, as to why the disease should occasionally run its course unattended by convulsions. Schmorl's explanation is that the eclamptic toxin is analogous in its action to certain drugs which have a stimulating effect when given in small doses, but cause depression and paralysis when administered in larger amounts. He is, therefore, inclined to regard such cases as manifestations of a more profound intoxication than occurs in the usual type of eclampsia, and ascribes the absence of fits to an overpowering of the central nervous system.

The truth of this hypothesis cannot be confirmed or denied until we have the poisonous principle in our hands. Meanwhile, it is of interest to study the anatomical changes exhibited by the seven cases reported with a view of ascertaining whether any organic lesion is constantly accentuated in non-convulsive eclampsia; and if so, what?

Pathological Summary.

Renal lesions were demonstrated in all cases, excepting that of Esch, in which the kidneys were not examined; but even in his case the clinical analysis of the urine afforded conclusive proof of the existence of a nephritis, as it showed a very large amount of albumin and numerous tube casts. In three instances there was evidence of a chronic nephritis with superimposed acute changes, while the three remaining cases presented only an acute parenchymatous degeneration. The intensity of the renal affection however, is notably inconstant, varying from a very mild, cloudy swelling of the epithelium to extensive destruction of tissue by hæmorrhage and necrosis.

The liver, without a single exception, presented characteristic necroses at the periphery of the lobule. Sometimes there was only a slight involvement of the organ, the necrosis not passing beyond the cells immediately adjoining the portal spaces. In other instances, large areas of the parenchyma were thrown out of function by degenerative processes and the extravasation of blood. Between these extremes, various gradations were noted, so that no connection can be established between the non-convulsive type of eclampsia and the intensity of the liver lesion. Similarly the heart and lungs

fail to show any more marked involvement than in typical eclampsia, although degeneration of the myocardium, and pulmonary œdema were observed in all the cases. Likewise, serous effusions into the peritoneal, pleural and pericardial cavities occurred in all the cases in which an especial autopsy note was made concerning the condition.

In contradistinction to the other organs, the brain in these cases was the seat of unusually severe lesions, which seem to be of such importance that I give a somewhat detailed account of the findings recorded in the literature.

SUMMARY OF PATHOLOGICAL ANATOMY.

No.	Reported by	Kidney.	Liver.	Spleen.	Pancreas.	Stomach.	Lungs.	Heart.	Serous Effusion.	Brain.	Bacteriology:
1	Schmorl.	Acute upon chronic nephritis.	Peri-portal necroses.	Enlarged.	No note.	Punctiform hæmorrhages.	Œdema.	Parenchymatous degeneration and punctiform hæmorrhages.	No note.	Hæmorrhage and œdema.	Negative.
2	...Do.....	Parenchymatous degeneration.	...Do.....	No note.	Focal necroses.	....Do.....	....Do.....	....Do.....	....Do.....	Dura distended by cerebrospinal fluid hæmorrhage.	....Do.....
3	....Do.....	Acute upon chronic nephritis.	....Do.....	....Do.....	....Do.....	....Do.....	....Do.....	....Do.....	....Do.....	Hæmorrhage into corpus striatum, cerebellum, pons and medulla.	....Do.....
4	Meyer-Wirtz.	Parenchymatous degeneration.	....Do.	....Do.....	No note.	Negative.	Negative.	Fatty degeneration.	Pleural and peri-cardial.	Cerebral apoplexy.	....Do.....
5	Esch.	Not examined.	..Do.....	Enlarged.	...Do.....	No note.	Œdema.	Punctiform hæmorrhages.	....Do.....	Hæmorrhage into lateral ventricles.	No note.
6	Slemons.	Acute upon chronic nephritis.	...Do.....	Coagulum in malpighian tufts.	... Do.....	Negative	Do.....	Parenchymatous degeneration.	Pleural, pericardial, peritoneal.	Details not obtainable.	Bacteroides capsulatus.
7	....Do. ...	Parenchymatous degeneration.	....Do.	....Do.....	Edematous.	Small fresh ulcer.	...Do.....	....Do.....	....Do.....	No examination.	Negative.

Schmorl's cases. No. 1: Meninges hæmorrhagic and œdematous. On the cortex multiple punctiform extravasations of the blood. In the central ganglia bluish red areas of softening, the size of a lentil. A similar focus in the left hemisphere of the cerebellum. No. 2: Dura under marked tension. Flattening out of convolutions. A hæmorrhagic area 3 to 4 cm. in diameter at base of left frontal lobe in subarachnoid space. Destruction of left olfactory and oculomotor nerves by hæmorrhage. Thrombosis of left cavernus sinus. Apoplectic focus, size of walnut in left frontal lobe. Multiple punctiform hæmorrhages over cortex. Areas of softening in cerebellum and central ganglia of variable dimensions, largest the size of a pea. No. 3: Punctiform hæmorrhages unusually abundant, and areas of softening throughout cerebrum, central ganglia, pons and medulla.

Meyer-Wirtz's case. Pia œdematous. Diffuse hæmorrhages on right side of temporal and parietal convolutions. 30 cc. of bloody fluid in posterior cranial fossa. Diffuse subpial hæmorrhages at base of brain in temporal region, as well as at boundary between cerebellum and pons. Blood clots on posterior surface of medulla and at point of exit of vagus. Lateral ventricles distended, containing bloody fluid. Substance of hemisphere pale, but of good consistence. Hæmorrhage into corpus striatum on right side, which extends into lenticular nucleus and internal capsule. Nucleus caudatus free, as also pedunculus cerebri. Extensive hæmorrhage in pons. Aqueduct of Sylvius and fourth ventricle filled with clots. Cerebellum negative.

Esch's case. Under posterior part of right parietal lobe there is a large extravasation of blood. On sectioning the brain, one finds single, punctiform hæmorrhages scattered throughout its entire substance. Hæmorrhage size of hazelnut in posterior part of right corpus striatum. Both lateral ventricles, and especially the right, are distended with bloody fluid.

The profound nature of the brain lesions noted here affords a probable anatomical and physiological basis for the unusual clinical course in this variety of eclampsia, and suggests at least two possibilites. In the first place the location and extent of the hæmorrhage into the brain substance could be such as to explain both the onset of coma and the absence of convulsions. The material at present available, however, speaks against the very frequent occurrence of this, and would rather seem to favor a second possibility, namely, that the phenomena in question are due to an increase in the intracranial tension, which in turn depends upon hæmorrhagic or œdematous changes in the brain or its enclosing membranes.

Rosenstein, who formulated his theory in accordance with the experiments of Traube and of Munk, formerly laid great emphasis upon the part played by increased intracranial pressure in the production of eclampsia. He held that increased arterial pressure and hydræmia were commonly observed in eclampsia; and that both of them caused an increase in intracranial tension; so that all of the symptoms of the disease could be interpreted as results of these changes. His hypothesis was ultimately abandoned, because the cerebral condition which supplied its basis was frequently lacking at autopsy. However it would seem that the brain lesions observed in these cases of eclampsia without convulsions strongly indicate, if they do not absolutely assure, a greatly increased intracranial pressure. Thus, hæmorrhage into the ventricles or beneath the meninges, œdematous changes in the brain

itself, or in the meninges have been found with great regularity. The dura has been seen to be markedly distended, the convolutions of the brain flattened out, and the cerebro-spinal fluid present in excessive amount; and all of these phenomena lead to the production of a high intracranial pressure.

The effect of an increase of tension within the skull is dependent upon the anæmia of the brain and medullary centers which follows it. This bears a very direct relation to the mean arterial pressure, as Cushing has shown that the blood supply to the brain is cut off when the resistance within the skull is greater than the force impelling the blood stream. The existence of this state of affairs may be accurately demonstrated only by comparing the pressure in the peripheral arteries with that in the cerebro-spinal fluid after trephining the skull and directly estimating the pressure within the cranium. However, no such observations have been made in cases of eclampsia without convulsions. Neither are we in possession of clinical data obtainable by a less radical procedure which would afford presumptive evidence of its existence, namely, a comparison of the pressure in the peripheral arteries with that in the spinal canal as determined by lumbar puncture. The importance of such observations in the future for the interpretation of the pathological physiology underlying eclampsia without convulsions is evident.

In our own cases the anatomical data at hand throw no light on the subject of intracranial tension. In the first case the intracranial conditions were not thoroughly studied at autopsy; while in the second, permission could not be obtained to open the skull. However, in this latter patient, who came under my personal observation, the clinical manifestations indicated the existence of an increased intracranial tension; as a marked elevation in blood pressure associated with periodic breathing is especially significant according to recent studies on Cheyne-Stokes' respiration.

Following the work of Cushing, which demonstrated in the event of an increase in the intracranial tension that the arterial pressure tends to rise and exceed the former, Eyster has been able to explain the association of "Periodic Breathing" with such conditions. The phenomenon would seem to depend upon "an alternation of anæmia and blood supply to the brain and medullary centers," as is shown by the blood pressure consecutively mounting above and falling below the line of intracranial tension, thus giving rise to the so-called Traube-Hering waves.

From his experimental and clinical work Eyster concludes that the existence of increased intracranial pressure in a patient may be definitely recognized when Cheyne-Stokes' respiration occurs "accompanied by a rise of blood pressure and an increase of pulse rate during the dyspnœic periods." The diagnostic value of these data and the importance of the changes in the eye grounds lately studied by Cushing and Bordley were not appreciated at the time our cases occurred, and we are, therefore, unable to make any statement concerning them. We do feel, however, that the clinical observations which were made, very strongly indicate a high tension within the cranium.

Diagnosis.

The clinical diagnosis in these cases has invariably been wrong. Most often the condition has been mistaken for uræmia, which is not surprising in view of the frequent history of long standing renal disturbance and the autopsy findings of chronic nephritis. Suicidal poisoning, cerebral syphilis and acute yellow atrophy were seriously considered several times, until the anatomical lesions revealed the true nature of the disease.

For the present we must admit that only the pathologist can make an absolutely positive diagnosis of eclampsia either with or without convulsions; and that his ability to do so will depend upon the demonstration of peri-portal necroses in the liver. This lesion, constituting the one constant feature of the disease, must be present to justify the diagnosis. The absence of it in the case lately reported by Reinecke effectually proves that his was not a case of eclampsia without convulsions.

Clinically, we remain unable to identify the disease positively at the bedside; since as I have already indicated, the obstetrician may meet on the one hand with various conditions besides eclampsia which are associated with convulsions and coma; while on the other, eclampsia may occur without giving rise to a single convulsive movement. Very fortunately, our inability to make an accurate clinical diagnosis is of but slight practical importance, since most of the affections with which eclampsia may be confused are manifestations of some variety of toxæmia of pregnancy and are, therefore, amenable to the same therapeutic measures. From a scientific standpoint, on the other hand, it is exceedingly important to differentiate, as far as possible, the several varieties of toxæmias, and at present this can be effected only upon a pathological basis. Failure to bear this in mind will result in great confusion and naturally delay the fuller recognition of our great ignorance and the subsequent development of more correct ideas.

Indeed, the anatomical evidence is so essential for the differentiation of every toxæmia of pregnancy that it is impossible to classify with certainty the cases reported by Lebenstein, Binder, Schlutius, and Jardine, in which recovery finally occurred. All of their patients were comatose for a time, having no convulsive seizures, while the urine changes were indicative of nephritis. It cannot be denied that these may have been instances of eclampsia without convulsions; but on the other hand, since positive anatomical proof as to their exact nature cannot be adduced, it would appear wiser to leave the diagnosis *sub judice*.

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NOTES ON NEW BOOKS.

Morris's Human Anatomy. Edited by HENRY MORRIS, M. A., M. B., F. R. C. S., and J. PLAYFAIR MCMURRICH, A. M., Ph. D. In five parts. (*Philadelphia: P. Blakiston's Son & Co., 1907.*)

The fourth edition of Morris's Anatomy, while still retaining to some extent its original character, has been in many respects profoundly altered. The Basle nomenclature has, generally in anglicised form, been used throughout. The sections on the muscles, central nervous system, organs of respiration, nose, ear, integument and perinæum have been practically rewritten, and the general arrangement has been somewhat altered to fit morphological, and in some cases physiological, rather than regional requirements; thus the old Section VII on the thorax has been omitted, the heart is treated with the blood vessels, the thyreoid and thymus glands are placed in a special section with the other ductless glands, and the mammary gland is treated with the integument.

Part I consists of the sections on general morphogeny, bones, and joints. Of these the first is entirely new, and is short but extremely concise and clear, and forms a very useful addition to the book. The section on osteology, which has always been known as one of the best features of this work, has undergone slight alteration, but is improved by the addition of several excellent figures. Unfortunately, the usefulness of this section has been considerably marred by the somewhat capricious rejection of many of the BNA terms. It may be urged that an author in writing or revising an article has a perfect right to use the terms which he thinks most suitable; here, however, the case is somewhat different.

The present edition of Morris is likely to be used by anatomists who recognize in the BNA an earnest endeavor to reduce a burdensome nomenclature to its simplest and most consistent proportions, and while they may not look upon it as perfect, any more than did the men who gave up so much time to its elaboration, they realize that much good may be achieved by its use, and that use alone will lead to future improvement. Under these circumstances, consistency becomes a point of the first importance, and the article, as it at present stands, is somewhat disappointing. Thus *Sinus tarsi* is as good a term as *Sinus pedis; superior* and *inferior* rami of the pubes are much preferable to *ascending* and *descending*. There seems no particular reason why the *epicondyles* of the humerus should be accepted rather than those of the femur. *Glenoid fossa* is not more desirable than *Mandibular fossa*. *Infratemporal fossa* has been practically rejected, at least it seems only to be used once to about nine times of *Zygomatic fossa*.

Professor Thompson uses *volar* and *dorsal* for the surfaces of the radius and ulna, but not for the borders; *medial* and *lateral* angles of the scapula are preferable to *superior* and *external*, and so are the terms *medial* and *lateral* for the surfaces and malleoli of the tibia and fibula. In the cases of *Tuberculum articulare, Foramen palatinum majus* and *Sinus transversus*, the object of uniformity has been defeated by the frequent use of the corresponding terms of the older nomenclature.

In revising his well-known and excellent section on arthrology, Mr. Morris has done little but employ the Basle terms. This has been done consistently, except in the cases of *Tuberculum articulare* and *Fossa infratemporalis* which, as in the previous section, have been overlooked.

Part 2 on the muscles and vascular system contains many improvements. The difficult task of entirely recasting the section on myology on a purely morphological basis, has been most successfully accomplished by Professor Bardeen. This change is very welcome; amongst numerous other advantages, we at last have the anconeus treated naturally as part of the triceps, and the oblique and transverse muscles of the thorax and of the abdomen considered together. In the case of the transversus thoracis, this would seem a good opportunity to have called the lateral attachment the *origin*, and the medial the *insertion*, and thus bring about conformity with the more important abdominal portion of the muscle.

Naturally there are a few points which might be improved in a later edition; for instance, in the description of the rectus sheath (p. 414) the terms *ventral*, *external*, and *front* have been used to denote the same surface of the muscle, where possibly more uniformity might have led to a clearer result. There also seems to be room for a more definite description of the upper part of the sheath.

The word *supine*, used on page 374 with regard to the position of the Antibrachium in quadrupeds should, no doubt, read *prone*. The whole section, however, is extremely well done, and contains much valuable information, drawn not only from an extensive knowledge of the literature, but also from the results of the author's own work.

Section V on the organs of circulation is principally distinguished by the part devoted to the lymphatic system, which, as might have been expected of Professor Sabin, who has done so much to increase our knowledge on this subject, is very much in advance of anything that has hitherto appeared in an English or American text-book on human anatomy. The part on the blood-vascular system has been improved by the addition of several figures, and by a good account of MacCallum's work on the architecture of the heart.

The statement on page 492 that the atrio-ventricular bundle "inserts into the ventricular septum" is misleading in two ways; firstly, because it can scarcely be called an adequate description of the extensive ramification of the ultimate fibers of the bundle in the ventricular walls, and secondly, because it implies a mechanical influence which this bundle may possibly possess, but of which we have no experimental proof. At present we know the atrio-ventricular bundle as a conductor only.

The significance of the so-called moderator band as a means of conveyance of a part of the right ventricular limb of the atrio-ventricular bundle from the ventricular septum to the anterior musculus papillaris, appears to have escaped notice. The constancy, or relative prominence of this band in the sheep as compared to man (referred to on p. 486), or, for that matter, its relative prominence in any mammal depends simply on the size of the anterior papillary muscle as compared to its fellows, and on the position of this papillary muscle with regard to the ventricular septum.

On page 623, in speaking of the articular arteries of the knee, the terms *medialis* and *media* (azygos) have both been translated *medial*, *middle* would have been a better rendering of the latter.

There is some inconsistency in occasionally using the terms *internal* and *external* for *medial* and *lateral* in referring to the plantar and cancaneal arteries; in adjusting this, Figure 465 requires re-labelling.

Part III deals with the nervous system and special sense organs. In the section on neurology, the part relating to the central nervous system has been entirely rewritten with considerable expansion. Professor Hardesty has handled this subject with admirable judgment, his article is sufficiently full without excess of detail, and the style in which it is written is a model of simplicity and clearness.

The excellent section on the eye has undergone little or no change. The parts relating to the ear, tongue, and nose have been very ably re-written by Professor Kerr, although in the two latter cases the employment of the terms *dorsal* and *ventral* in a proverbially difficult situation, has led to a result not entirely free from ambiguity. Thus the following description does not seem quite clear. "The external nose is shaped like a triangular pyramid. At the forehead, between the eyes, is the root of the nose, and from this extending inferiorly and ventrally, is a rounded ventral border, the dorsum of the nose, ..."

The direction *ventrally*, in this case, is somewhat arbitrary, it is obviously used as opposite in direction to the back of the head which is considered as dorsal; we have only to consider the top of the head as dorsal (which would be equally valid) to make the directions *ventrally* and *inferiorly* coincide. In the tongue the tip has been considered as *ventral* and the root as *dorsal*, whereas the dorsum might equally well, perhaps better, be considered as dorsal and the attached surface as ventral. Having admitted, as Professor Kerr does, the directions *superior* and *inferior*, the use of the terms *anterior* and *posterior* would have added considerably to the clearness of the descriptions.

In Part IV, the section on the organs of respiration has been excellently re-written by Professor Terry. "The structures at the pelvic outlet," a rearrangement of the old part on the Perinæum which it replaces, has been very ably written by Professor Thompson, and is now practically a new article, as is also Section XII on the skin and mammary gland by Professor Kerr.

The remainder of this volume has been revised without any very radical alteration. The section on the organs of digestion, revised by Professor Huber, has undergone little change, except for some additions on development which are excellent, particularly the accounts of the development of the peritoneum and intestine, which together replace the well-known section on the evolution of the peritoneum of former editions. Dr. Huber has also added notes on development in the section on the ductless glands and a short account of the parathyroids.

Professor McMurrich in revising the section on the genito-urinary organs, has rewritten the account of the development of the reproductive organs. Henle's section of the female pelvis in which the uterus is retroverted, has been replaced by a figure in which the parts are normal.

Part V on surgical anatomy has been thoroughly revised, and, like everything from the pen of Mr. Jacobson on the relations of anatomy to surgery, it is full of interest. The extraordinary amount of practical information crowded into this section without the slightest ambiguity of expression, marks it as a piece of work of a very high order.

The adoption of the Basle nomenclature for the first time in a text-book on human anatomy in the English language, is a most important step, and one on which the editors are to be congratulated, particularly as in doing this they have produced an extremely good work which deserves to be widely used. H. D. S.

International Clinics. Vol. III, 17th Series. (*Philadelphia and London: J. B. Lippincott Company, 1907.*)

These "Clinics" are so well known and so justly appreciated by the profession that little more need be said about this volume than enough to draw attention to its appearance. Twenty-five authors, nine of whom are foreigners, have contributed the 25 papers of this volume, dealing with treatment, medicine, surgery, gynecology, genito-urinary diseases, ophthalmology, neurology, dermatology, and pathology. The editors are to be complimented on their success in the preparation of the "Clinics," in keeping

an even balance of all the different departments mentioned. No section of medicine, taken in its broadest sense, receives more or less than its due attention. All the papers submitted are timely, and many of them are excellent reviews of the present status of certain problems not yet elucidated, on which much work is being done, and which are because of their inherent difficulties little understood by the general practitioner, for instance Leo Loeb's article on the "Inoculability of Tumors, and the Endemic Occurrence of Cancer." R. N.

Manual of the Diseases of the Eye, for Students and General Practitioners. By CHARLES H. MAY, M. D. Fifth Edition, Revised. (*New York: Wm. Wood & Co., 1907.*)

This excellent manual which, since its publication in 1900, has reached a fifth edition and has been translated into several foreign languages, is too well known to need extended notice. The remarkable success which it has met with and its popularity abroad as well as at home are to be attributed, it would seem, to its conciseness—its "multum in parvo" character—the convenient arrangement of the subject matter, and perhaps in no small degree to the great number and excellence of the illustrations. These unquestionably add materially to the value of the book, and, except for the somewhat "florid" character of the colored plates representing the superficial diseases of the eye, are deserving only of commendation.

In view of the fact that the work has passed through five editions, and that "every page," as the author tells us in the preface to the present edition, "has been carefully examined," we have been somewhat surprised at the number of "slips" which a not very critical perusal of the volume has brought to light.

For example, in discussing the treatment of sympathetic ophthalmitis, the author tells us on page 161 that "enucleation of the injured eye has no effect upon the progress of the disease," while on the next page he advises enucleation under certain circumstances, "since its [the exciting eye's] presence may aggravate the condition of the sympathizing eye."

Again, the definition of "ametropia" on page 270 is not broad enough to include astigmatism, which, of course, it should be. The statement (page 276): "If the patient reads 20/xx, we may assume the absence . . . . . of astigmatism" is erroneous, and it would not be true, even if the author had qualified it by saying "astigmatism of significant amount."

Again, in the description of the optometric use of the ophthalmoscope by the direct method (page 279) we read: "The examiner, if ametropic, corrects his error by wearing suitable glasses . . . . or by subtracting the amount of his error from the result which he observes in the examination." Whether the examiner's error should be subtracted from or added to the ophthalmoscopic finding will depend, of course, upon the nature of his own and the patient's refractive fault. Thus, if the examiner with $2D$ of myopia is able through a $+4D$ lens to see distinctly the details of the patient's eye-ground, the patient's hypermetropia is $4D + 2D = 6D$, not $4D - 2D$. In an algebraic sense the author's statement is correct, but only if one thinks of myopia as having a negative and of hypermetropia as having a positive value.

The diminution in the acuteness of vision we are told (page 302) "is least with simple astigmatism, more with compound astigmatism, most with mixed astigmatism." It seems hardly necessary to point out the error involved in this statement, for everyone who has to do with faults of refraction knows that in a high grade of simple astigmatism vision is commonly more markedly impaired than in a relatively low degree of compound or even mixed astigmatism.

On page 348 "orthophoria" is given as one of the "various forms of heterophoria." The statement at the top of page 352 should read: "But if there is [*lateral*] heterophoria," etc. In this connection, furthermore, we would suggest that in employing the Græfe vertical diplopia test, it is much better to use a 4-degree prism for the distance and a 7-degree prism for the near than to use one of 10 degrees for both far and near, as the author advises, since the possibility of error from inexactness in the position of the prism increases with the strength of the prism employed.

Weber, we are inclined to think, would be somewhat surprised if told that Fig. 85 (page 59) represents his probe-pointed canaliculus knife.

However, these errors are of minor importance, are easily rectified, and detract but little from the general excellence of the book. S. T.

Genito-urinary Diseases and Syphilis. By H. H. MORTON, M. D. Second edition. (*Philadelphia: F. A. Davis & Co., 1906.*)

It is unfortunately true that the standard of the average American text-book on genito-urinary diseases is rather poor, but the above volume is certainly not destined to raise the already low standard.

We are advised in the preface to this new edition that the rapid advances in many fields of genito-urinary surgery have rendered imperative a revision of the old edition. It is fortunate that the author has acquainted us of the fact that advances have been made, as a perusal of this new edition fails to impress one with that fact.

The anatomical material is handled in the most elementary and school-boy fashion and often most curious anatomical statements are made. For instance, in dealing with the anatomy of the urethra (page 23) we are told "the urethra is a tube open at both ends." This tube the author divides into three regions, the "anterior or pendulous urethra, the membranous and the prostatic urethra." This division of the urethra we must admit is quite original, for it is not usual in works on the anatomy of the urethral tract to speak of the pendulous as synonymous with the anterior urethra. According to this division the pendulous portion extends back to the membranous which, to say the least, is a very curious and not at all accepted idea as to what constitutes the pendulous urethra. On page 24 the author presents a most wonderful anatomical diagram of the urethra and bladder. In this diagram the ejaculatory ducts are shown traversing an empty space between the prostate and the posterior wall of the bladder to open in the prostatic urethra without passing through the prostate gland. Furthermore, the apex of the prostate is the only portion of the gland in any way connected with the urethra, while the suspensory ligament is shown attached to the lower end of the pubis and the anterior part of the prostatic urethra.

Such mistakes are absolutely inexcusable and almost inconceivable.

It is not our purpose to take up in detail the various points deserving of criticism, but we cannot help referring to the chapter on chronic prostatitis. On reading the symptoms of chronic prostatitis as handled by the author, one would imagine he was dealing with the text-book of 50 years ago rather than a revised, supposedly up-to-date edition of a genito-urinary text-book.

We have referred to these few points in the volume, not because they are the only ones requiring criticism, but because they give some idea of the character of the book. It is a volume which certainly does not deserve a position in the library of the student or practitioner.

Green's Encyclopedia and Dictionary of Medicine and Surgery. Vols. I, II, and III. (*Chicago: W. T. Keener & Co., 1906.*)

These three volumes are direct descendants of the *Encyclopedia Medica*, but contain, in addition to the elaborate articles of that work, many new and more distinctly dictionarial paragraphs. That is to say, the editor has aimed, as the title of the work indicates, to produce a dictionary and an encyclopedia in one; he has

had, obviously, great difficulties to contend with in attempting to keep such extensive material within dimensions that were at all manageable; but he has succeeded notably. The articles are concise and complete; no words are wasted in them, and it is difficult to see how the necessarily limited space allotted to the contributors of such a work could have been better used.

One of the most useful features of the encyclopedia is the admirable system of what the editor calls "illuminating cross references"; it is a feature which must have involved an endless amount of Dr. Ballantyne's time and energy; and its excellence proves that the editor has been something more than a figure-head.

Such a work as this encyclopedia must, of course, be incomplete and unsatisfactory in places. When one considers that it must treat such subjects as "Anthropology," and "Linguistics," and "Physiology of the Brain" within the limits of a very few printed pages, one realizes that it is absurd to expect of it the completeness which is possible for the average text-book. The choice of essentials has, however, been wisely made.

Metabolism and Practical Medicine. By Carl von Noorden, Professor of the First University Medical Clinic, Vienna. Anglo-American Issue under the Editorship of I. Walker Hall, Professor of Pathology, University College, Bristol, Pathologist to the Bristol Royal Infirmary. Vols. 1 and 2, pp. 525. (*Chicago: W. T. Keener & Co., 1907.*)

The timely appearance of this comprehensive work on metabolism in its direct bearing on practical medicine will be heartily welcomed by all who are interested in this extremely important branch of medical science. While some of the most important results thus far attained in the field of metabolism have been contributed by Americans working in purely scientific institutions, the practical medical men of America, with few exceptions, have been singularly slow in entering this very promising field of work. The appearance of this work will probably stimulate much needed investigations in this field as many important and practical questions are awaiting solution. The work will apparently be complete in three volumes of which the reviewer has only two before him. The various articles were written by well-known German authorities and rendered into English by a corps of translators. Volume I deals with the physiology of metabolism. The general style in this volume is not clear and in places unscientific. Numerous errors are also to be found in it of which only a few can be noted here. On p. 154 the statement is made that "Fructose and glucose are thereby first transformed into grape-sugar." On page 157 it is stated that acetaniiid contains two atoms of carbon. It is impossible in this case to make out what the author had in mind. Later in the same paragraph the statement occurs that "'carbohydrate fat' is fairly stable, and melts early with higher temperatures, ..." In the discussion of the acetone bodies the term acetic acid is used throughout in place of aceto-acetic acid, although the formulas are correct for the latter. Sentences such as the following are not sufficiently infrequent in the first volume. "What part is played biologically by the valence of albumin (regarded both as a sub-alkaline and as an acid-binding body) which has been discovered by Loewy's experiments is, for the main part, unknown."

The second volume is written on an altogether higher plane and will be a valuable addition to any medical library. It deals with the medical phases of the subject. The chapters bear the following headings: Hunger and Chronic Starvation, Overfeeding, Fever and Infection, Diseases of the Stomach and Intestines, Diseases of the Liver, Diseases of Respiration and Circulation, Diseases of the Blood, Diseases of the Kidneys.

In this volume a mass of data widely scattered in the literature is presented and the discussions are comprehensive and lucid. At the end of each discussion a good bibliography will be found. The second volume is to be especially recommended to the medical public.

A. S. Loevenhart.

The Cause and Prevention of Beri-Beri. By W. Leonard Braddon, M. B., B. S., F. R. C. S., State Surgeon, Negri Sembilan, Federated Malay States. (*New York: Rebman Company, 1907.*)

In his preface the author states that "this work consists chiefly of a report presented to the Colonial Office in May, 1904. . . . . In the present work I have sought as far as possible to omit all mere opinions, and to present the reader with the evidence of *facts*. If, therefore, it seems presumptuous to claim, as I do, that in this book a problem which has vexed medicine for centuries receives solution, that the cause and prevention of beri-beri are clearly and certainly shown, the appeal is not to the author's opinions, but to the facts recorded for justification." It is doubtful whether all the readers of this work will agree with the author in thinking that he has solved the problem, but none can fail to recognize the large amount of work the author has put into his task, and the care with which he has studied the subject. The reviewer feels, however, that as with Hutchinson's theory as to the decayed fish origin of leprosy there is still a link in the chain wanting to prove absolutely that bad rice is the cause of beri-beri. It is perhaps not quite fair to state simply the author's conclusions in this question, but it is not possible to consider each one and discuss it at length. This would necessitate such a review of the subject as the author has given us. It is done, however, to interest other readers in this report, which is a most admirable one, for which the author deserves the highest credit. It is to be regretted that the book will probably not be much read in this country where as yet beri-beri is practically unknown, but it will be of service to those who are interested in studying obscure problems of this nature by showing them how a first-class report should be written. Dr. Braddon's conclusions are as follows:

1. "Stale decorticated (white) rice, therefore, at times contains a poison, the effect of which is to produce beri-beri."

2. "The agent which produces the poison in rice is specific of, or peculiar to, that grain."

3. "The beri-beri poison is not preformed (or not present in quantity sufficient to cause symptoms) in normal fresh rice-seeds, but is adventitious."

4. "The pericarp of rice, like the seeds when fresh, contains little or no poison."

5. "The formation of poison in stale rice is due to the action of a specific agent upon the dead seeds."

6. "The poison of stale rice has an antecedent in fresh rice. The agent must be, therefore, some ferment or parasite or epiphyte peculiar to fadi [the raw grain]."

7. "The beri-beri poison is probably an alkaloid which is stable and non-volatile, and resembles atropine and muscarine in some of its effects."

8. "The formation of poison in stale rice is probably due neither to fermentation nor to bacteria, but to the growth in it of a special fungus."

9. "The beri-beri producing fungus of rice is probably a surface-parasite, or epiphyte affecting the seed saprophytically after decortication."

10. "The specific fungus of beri-beric rice is, like that of toxic rye and lolium, probably a parasite affecting the surface of the seed."

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COMPARATIVE SURGERY.

THIRD SERIES OF REPORTS.

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(*From the Hunterian Laboratory of Experimental Medicine.*)

Numerous requests for further data in regard to the methods of teaching operative surgery in the Hunterian Laboratory have come from various parts of the country where similar courses are being formulated or have already been introduced into the curriculum. I shall take this opportunity of replying to some of these inquiries.

The three main purposes for which the laboratory was established are: (1) investigation, particularly along the lines of morbid physiology and comparative pathology; (2) the treatment of the surgical maladies common among the smaller domesticated animals; and (3) the training of third year students in such fundamental principles of actual surgical handicraft as anæsthesia, asepsis, hæmostasis, and the proper handling of living tissues and organs. In the accomplishment of these objects considerable overlap is possible; thus, for example, the strictly veterinary work gives opportunities for the instruction of junior students in modern surgical methods and furnishes at the same time abundant occasion for investigation—opportunities exactly comparable to those offered by the conditions of disease encountered in a hospital for human beings.

We are often asked what attitude is held by the local veterinarians toward our seeming encroachment on their particular field of work; and it may be said that we have received encouragement and friendly co-operation from many of these gentlemen. Most men engaged in veterinary work find it difficult or impossible to secure sufficient training in modern methods of aseptic surgery to enable them to carry out with a minimum of risk—not to mention the minimum of suffering—even the simpler operations such as spaying, the radical cure of hernia and of vaginal prolapse, the removal of superficial tumors and the like.

It is remarkable that the surgical maladies of our domesticated pets continue to be treated in ways which are exactly comparable to the crude and painful procedures to which human beings were necessarily subjected in the dreadful days before anæsthesia and before Lister—days when operations were largely limited to lesions external to the body cavities, when escharotics were used, the actual cautery, crushing clamps and similar harsh measures. There can be no better illustration to-day of the strides in surgical technique which the last fifty years have seen than the comparison of a clean, painless ovariotomy as performed by a skilled surgeon and the corresponding operation on a dog by an untrained veterinarian—in the latter case a struggling animal suspended by her hind legs; often no anæsthesia or skin preparation; a bilateral opening through which the ovary on each side is withdrawn by an unclean finger introduced into the peritoneal cavity, to be

subsequently avulsed from its attachment without other effort at hæmostasis. On the one hand, experience gained almost entirely from animal experimentation is used constantly for the benefit of mankind; but on the other the animals whose kin have been sacrificed to supply this experience have as yet profited nothing thereby.

I do not mean that such measures as this are invariable with veterinarians, for there are doubtless notable exceptions among the graduates from the better schools in other cities as there are here in Baltimore; but from what we have seen of the end results of surgery as it is generally practiced upon the lower animals it is safe to say that these methods represent those commonly utilized. It is not because veterinarians are heartless—surgeons in times gone by, by force of necessity employed similar procedures; it is because the majority of them have had no opportunity to learn other and more humane methods of treatment. After attending some of our surgical exercises as onlookers a number of these men have begun to send their more serious surgical problems for us to solve; and we anticipate, furthermore, in the coming graduate course in the spring, to have a table set aside for their use, so that a selected few who are desirous of acquiring experience in modern aseptic methods may do so free of expense. It is purposed also to extend the privilege to a number of these men of operating on their own patients in the laboratory; in this way we shall doubtless see a larger number of the serious maladies at present regarded by most veterinarians as surgically incurable, and we shall acquire at the same time more pathological material for comparative study—a mutual benefit. It means, perhaps, the beginning here of veterinary work under university auspices, and we feel that, by enrolling the interest of the men already engaged on this work, we can be of service not only to them, but indirectly can spare much suffering on the part of the lower animals.

Although during the past school year we were under no direct affiliation with the veterinarians, nevertheless an increasing number of animals suffering from surgical maladies have been referred to us, and there have been admitted to the laboratory-clinic instances of the following conditions. There has been an unusual variety of neoplasms. In addition to a number of the mixed tumors of superficial glandular origin, such as were described by Dr. Ortschild in his paper two years ago, we have seen a primary osteosarcoma of the radius; epitheliomas on the thoracic wall and neck; a primary melanotic sarcoma of the scrotum; a case of multiple fibromata of the vaginal wall; a malignant papilloma of the kidney; a primary sarcoma of the heart; a mammary cancer in a cat, etc.[1] There have been a number of cases of fracture, simple and compound, of the extremities and of the skull; cases of "cancrum oris;" a suppurative infection of the frontal sinus; strangulated hernia; cases of spinal paraplegia, both following trauma and secondary to distemper; a second case of chronic endocarditis with bloody ascites; a number of opthalmological conditions necessitating enucleation or cataract operations, and so on. In addition several animals have been sent to us to be spayed.

These patients with pathological lesions, together with the animals evidently suffering from fatal maladies which are brought to us from time to time by their owners to be humanely sacrificed, have supplied us with considerable material for surgical work, but as yet the number of admissions derived from these two sources has proved insufficient for the necessary amount of class material—this is partly due to the fact that many of the patients are valuable dogs whose ailments are much too critical to be turned over to students who as yet may be surgical novices.

Consequently we have been compelled to use for surgical teaching—the operations being carried out with all respect for modern surgical precautions—certain vagrant animals suffering from no other maladies than the minor ills which affect the entire stray canine population; and animals from this source are likewise used for experimentation, the results of which should indirectly prove of benefit not only to those domestic animals more fitted to live, but, in many cases, from a comparative point of view, even to human beings.

It is this aspect of the work concerning which we are most frequently consulted, and at the present day I should not feel justified in advising the inauguration of a purely operative course in any medical institution apart from the associated veterinary work, even though the training is of the greatest possible value to students. I doubt not that the time will come when intelligent legislation will provide for the needs of medical schools in supplying such lower animals as are necessary for research and teaching, just as it has already done in regard to anatomical material. It was absolutely essential to have bodies for dissection, and until suitable laws were passed and an Anatomical Board was established abuses were flagrant; it is equally essential to employ living animals for the furtherance of our knowledge of disease and its methods of treatment, but as yet there are no laws which recognize this fact. The natural solution of the difficulty would be to have the vagrant animals, which are at present gathered in at the city's expense and sacrificed at the pound, turned over, if unclaimed, to, let us say, a Board of Veterinarians for use in proper ways in the veterinary and medical schools, and I doubt not but that the matter will at some future time be decided in this way.

For the present we must continue to use stray animals of the class that otherwise find their way to the city pound, and these animals as a rule are easily distinguished from those which have homes.

Personally I cannot but think that an ultimate death under anæsthesia in a laboratory-hospital, where in the interval of sojourn painstaking care for the health and wellbeing of the

[1] Fragments from many of these tumors have been transplanted into vagrant animals in the laboratory without any subsequent growth from the grafts; we have encountered none of the cases of lymphosarcoma which afford so favorable an opportunity for the study of malignant disease by transplantation. It is quite possible that had it been feasible to graft tissues into a larger number of animals—rarely more than four were used on each occasion—we might have succeeded in starting a successful series of transferences.

inmates is, if for no other reason, necessary for the success of operative measures, must be a less tragic death than the usual one from violence, disease or starvation, to which most of these animals ultimately succumb on the streets.

Certainly no one should enter upon such work without being fully alive to its moral responsibilities and fully informed in regard to the arguments advanced, doubtless always with benevolent intent, by those who abhor for any purpose whatsoever experimentation upon animals. No student should be allowed or should allow himself to undertake researches involving the life of animals, any more than he should allow himself or be allowed to shoot game for sport—even for food or wearing apparel—unless the right of the action has been clearly settled by competent authority, and he feels that the end in view justifies the sacrifice of animal life. Particularly from the standpoint of vivisection this matter has always been carefully laid before each group of students, and they are urged to read such volumes on the subject as have been published by Stephen Paget,[2] Harold C. Ernst;[3] the minutes of evidence before the earlier commission as well as those taken before the Royal Commission on Vivisection,[4] which more recently has been sitting in London; and the report of the hearing before the Senate Committee, in February, 1900, in Washington.[5]

Contrary to the common view that an experimentalist becomes callous to animal suffering, I think the reverse is true and that no one holds in abhorrence the infliction of unnecessary pain upon animals more than do those who live in a laboratory, surrounded by them. It may not be out of place to append here our laboratory rules:

1. Animals admitted to the laboratory, whether as vagrants or as veterinary patients, shall receive all possible consideration for their bodily comforts and their surroundings shall be kept in the best possible sanitary condition.

2. In all operative work conducted in the laboratory the same aseptic precautions shall be taken and the same efforts made to avoid the infliction of any pain by the proper use of anæsthesia that are observed in a hospital for human beings.

3. No operations or experimental investigations shall be undertaken except with the sanction of one of the directors of the laboratory, who shall hold himself responsible for the fact that the procedure is justified by the end in view and that it is performed in such a manner as to minimize all discomforts, particularly in those cases in which the animal is allowed to recover from the anæsthetic.

4. Records shall invariably be kept in regard to all operative or experimental investigations and these records, as well as all pathological material, shall remain the property of the laboratory.

5. No animal, whether a patient or the subject of an investigation, when afflicted with an incurable or lingering illness, shall be kept alive, unless at the solicitation of the owner, in whose absence judgment in the matter shall rest with either of the directors of the laboratory.

6. An autopsy shall be performed in all cases of death occurring in the laboratory, and these autopsies shall be conducted with the same respect and formality observed in the pathological department of a general hospital, and the findings shall be recorded in the laboratory records.

7. Vagrant animals brought to the laboratory and purchased there shall be held as at the city pound for at least forty-eight hours, and shall be returned to their owners if claimed and identified.

We have learned from some other places, where the effort has been made to establish courses similar to those given in the Hunterian Laboratory, that some local opposition has been aroused among those who have little sympathy with biological or surgical advancement at the expense of animal life; but I feel sure that with precautions such as we have taken to remove the objectionable feature from the work and with the demonstration that it is for the actual benefit of the fittest to survive of the class of animals that are used, there will be no occasion whatsoever for criticism.

I have felt that it is especially needful for the graduates who take the operative course during the spring months—many of whom after their return home endeavor to keep themselves surgically expert by occasional operations upon animals—to carry out this work openly and in such a way that there can be no occasion for unreasonable opposition. Their townspeople can be easily made to understand the wisdom of a demonstration that they can safely conduct operations upon animals before undertaking similar procedures upon man—and many a physician in a small community, by force of circumstances, must in emergency not infrequently carry out more or less major operations.

During the past year all told, a large number of animals, chiefly dogs, cats and rabbits, have passed through our hands at the Hunterian Laboratory, which has come to be a distributing centre for the other laboratories of the school where, from time to time, experimental observations must needs be made. Inasmuch as when housed under one roof and cared for by trained attendants much better accommodations are assured than if an attempt were made in separate departments to have small animal-houses, by this arrangement not only do the inmates receive better attention and are kept in better health, but also, owing to methods of overlap, there is an actual saving of animal life, since the surgical procedures are much more likely to be conducted without fatalities in an operating room where modern surgical methods are in constant use than in laboratories where there may be a less strict technique. In this way it is often possible to utilize, for purposes of surgical teaching, such procedures as the making of fistulæ, the extirpation of organs and the like, when animals with these lesions are needed for demonstration or research in the physiological laboratory.

[2] Stephen Paget: Experiments upon Animals, with an Introduction by Lord Lister. G. P. Putnam's Sons, New York, New Edition, 1903.

[3] Harold C. Ernst: Animal Experimentation; A Series of Studies Indicating its Value to Biological and Medical Sciences. Little, Brown & Company, Boston, 1902.

[4] Royal Commission on Vivisection. First, Second, and Third Reports of the Commissioners. Minutes of Evidence. London, 1907. Wyman & Sons, Ltd.

[5] Hearing before the Senate Committee of the District of Columbia, Feb'y 21, 1900, on S. 34, for Future Prevention of Cruelty to Animals in the District of Columbia. Senate Document 26, 56-1, serial 3868.

The course of twenty exercises given for advanced students or for graduates is somewhat as follows; the methods used in presenting the subjects for the individual exercises have been described in another article:[6]

1. General surgical principles and conduct of operations; preparation of material, of gauze, sutures, etc.; asepsis and antisepsis; simple median abdominal exploration for the removal from the stomach of a foreign body previously inserted. *Gastrotomy.*

2. Variety of abdominal incisions and methods of closure. Removal of cæcum through an intermuscular (gridiron) incision. *Appendectomy.*

3. Surgery of the kidneys, with methods of exposure and exploration of these organs. *Nephrotomy* and *Nephrorrhaphy.*

4. Physiology of the gastric secretion, with review of Pawlow's, Cannon's and others' work. Development of the operation of *Gastrostomy.*

5. Physiology of the duodenal secretion. Surgery of the pancreas and biliary passages. *Cholecystectomy.* Exposure of pancreatic ducts by transduodenal incision. Pawlow's pancreatic fistula for more advanced students.

6, 7, 8. The development of the operation of *Gastroenterostomy.* (1) Simple anterior method with lateral anastomosis and its deficiency, as seen from subsequent results. (2) The posterior operation by a short-loop or no-loop method. (3) Roux' "Y" gastroenterostomy.

9. Non-malignant pyloric stenosis. Gastric ulcer; its course and methods of treatment in various stages. *Pyloroplasty.*

10. The various methods of *Herniotomy.*

11, 12. The general technique and principles of amputations by slow methods of dissection with complete hæmostasis. (1) *Amputation at the hip.* (2) *Interscapulo-thoracic amputation.*

13. Malignant disease of the stomach. *Pylorectomy.*

14, 15. Intestinal resections and the various methods of anastomosis. The physiology of intestinal digestion. Segmentation and peristalsis. (1) *Lateral entero-enterostomy.* (2) *End-to-end entero-enterostomy.*

16. The physiology of the large intestine; its surgical lesions and their operations. *Resection of cæcum.*

17. Surgery of the chest, heart, and blood-vessels. Principles of intrathoracic work; artificial respiration, etc. *Resection of rib. Thoracotomy. Anastomosis of blood-vessels.*

18. The general principles and technique of spinal operations. The physiology of spinal lesions, etc. *Laminectomy.*

19. Technique of cranial operations. Cerebral localization. *Craniotomy;* with cortical stimulation.

20. Gun-shot wounds of the chest and abdomen.

A course of exercises such as this can be indefinitely prolonged and variously modified. When conducted, however, not for the purpose of teaching any particular operative procedures, but rather for the purpose of enabling the student to acquire technical facility in exposing and handling the different living tissues and organs, and experience with the healing of wounds, such a course should suffice to firmly establish the necessary surgical resources which not only make of him a safe assistant, but which will enable him to undertake with comparative safety the treatment of almost any minor surgical ailment, and at the same time will give him a very good chance of successfully carrying through such major operations as he may in emergency unavoidably be called upon to perform.

HARVEY CUSHING.
J. F. ORTSCHILD.

[6] Instruction in Operative Medicine: with the Description of a Course given in the Hunterian Laboratory of Experimental Medicine. Johns Hopkins Hospital Bulletin, 1906, Vol. XVII, p. 123.

XII. BALANO-POSTHITIS IN DOGS.

By J. T. GERAGHTY, M. D.

It has been noted for some time that 75 to 80 per cent of the male dogs brought to the Hunterian Laboratory have what was supposed to be a urethral discharge. It has been a prevalent lay opinion that this discharge in dogs is similar in nature to the gonorrhœal urethritis of man, but whether this view is generally held by veterinarians we have been unable to learn.

It is well known that prostatic hypertrophy in dogs is not a rare condition, and the fact that they, in common with man, are supposed to be frequent sufferers from urethritis, has been used as an argument in favor of the inflammatory nature of prostatic hypertrophy. Hence the investigation of this subject was of interest from the standpoint of comparative pathology.

On examining the afflicted dogs a rather thick, greenish-yellow discharge is seen to ooze from the preputial orifice. On retracting the prepuce the glans is found bathed in this thick secretion, but none can be milked or squeezed from the urethra. The mucous membrane of the prepuce and the glans presents no macroscopic evidence of inflammation and to all appearances seems entirely normal. There is no redness, erosion or œdema of the tissues, while the surface epithelium appears to be intact.

Smears made from the discharge show a few pus cells and an enormous number of bacteria. The prevailing type of organism is a short, slender bacillus, although a variety of cocci and bacilli of other forms are present.

In order to determine more definitely the character of the infection and to exclude if possible the presence of an infection of the urethral mucous membrane, blocks of tissue were taken from the prepuce, glans and urethra.

Prepuce.—Sections made from its inner or mucous surface show an intact epithelium which appears to be normal in every respect. Between the epithelial cells, however, numerous polymorphonuclear leucocytes are seen, and beneath the epithelium there is evidence of an inflammatory reaction; for we find a considerable infiltration of round cells and leucocytes, though

there is very little if any fibrous tissue formation. Beneath the epithelium also numerous lymphoid follicles are found. The inflammatory reaction often surrounds these follicles but does not invade the lymphoid tissue itself. The inflammatory process does not extend deeply into the subepithelial tissue and appears to be a very low grade of infection.

Glans.—Examination of the sections from the glans shows a somewhat different picture from that noted in the prepuce. The epithelium is intact and apparently normal, aside from the fact that occasional leucocytes are seen lying here and there between the epithelial cells. There is, however, no subepithelial inflammation as seen in the prepuce, the leucocytes having apparently wandered in from the surface.

Urethra.—Numerous sections were made from different parts of the urethra, penile, membranous and prostatic, and in every instance the mucous membrane was entirely normal, there being no evidence of any inflammatory reaction whatsoever.

These observations seem to demonstrate that the penile discharges so common in dogs and generally considered to be due to a urethritis are, on the contrary, due to a mild grade of balano-posthitis.

XIII. PROSTATIC HYPERTROPHY AND PROSTATIC ATROPHY IN THE DOG.

By J. W. Churchman, M. D.

An examination of the rather meager literature on prostatic hypertrophy in the dog shows that the condition, though well recognized, has received scant attention in its histological aspects. Marked variations in the size of the dog's prostate are mentioned as frequent by Ellenberger and Baum; and Kitt refers to prostatic hypertrophy, both adenomatous and fibrous, as of common occurrence in old dogs. Neither writer, however, pays much attention to the microscopical picture, though Kitt refers to the frequency of prostatitis in dogs—both catarrhal and purulent—and to its presence in the hypertrophied prostate. It is an interesting fact that suprapubic prostatectomy had been done by a German veterinarian (cited by Loumeau) on ten dogs, for prostatic hypertrophy, before the operation, commonly known as Freyer's operation, had been done on man.

The normal prostate of the dog.—The dog's normal prostate (Fig. 1*C* and Fig. 2) is composed of numerous lobules seen to be sharply separated, when examined microscopically, by fibrous tissue trabeculæ. The striking feature about the gland is the richness of its acinous labyrinth; the picture seen in human hypertrophy is suggested, except that the acini are not dilated and are lined by normal epithelium. The richness in glandular tissue is, however, in marked contrast to the normal human gland. The epithelium lining the acini is of the high columnar type.

Another striking feature often seen in the prostate of the dog is the infiltration of the interacinous connective tissue with round mononuclear cells. I am not sure just how frequent this condition is, but there is no doubt that it very often occurs. A few polymorphonuclear leucocytes also take part in the invasion; but the majority of the cells are mononuclear and vary in size—the smaller cells having heavily stained granular nuclei, the larger, faintly stained nuclei with one or more nucleoli. Lymphoid prostatis, in other words, is apparently a frequent finding in the "normal" prostate of the dog.

Prostatic hypertrophy in the dog.—The specimen of hypertrophy described in this communication was obtained at autopsy on a vagrant dog which had been sacrificed under ether owing to his poor condition. The animal was a large, shaggy dog of unknown age. For the twenty-four hours after his admission and up to the time of his anæsthetization he moaned and cried incessantly. This fact I was at first tempted to explain as a symptom of urinary retention due to the prostatic hypertrophy actually found at autopsy; but subsequent study of the specimen showed such an explanation to be unwarrantable. No other facts in the previous history of the animal are at hand. The specimen removed consisted of prostate, bladder, ureters and vasa deferentia. The kidneys were macroscopically normal.

The *prostate* (Fig. 1*B*) was large, nearly round, symmetrical, quite regular in contour and with a definite median groove. It measured 5 x 4.5 x 3.5 cm., and was much larger than the bladder, which measured 3.5 x 4.5 x 2 cm. The neck of the urethra commonly seen in the dog between the bladder and prostate was encroached upon by the prostatic hypertrophy. The gland was soft and homogeneous. There was no lobulation nor anything to suggest the spheroids of human hypertrophy. On section of the hardened gland, the cut surface showed the same picture throughout and there was no differentiation between central and peripheral portions. The surface was smooth and homogeneous except that it was dotted throughout with dilated ducts varying in size from small cysts just visible to the naked eye to larger ones nearly 1 mm. across. The appearance suggested fibrous tissue rather than a tissue rich in cells—in contrast to the appearance of the cut section of a normal prostate, which is quite cellular. The prostatic urethra was large, patulous and normal in shape. The prostatic orifice was normal and its mucosa was continuous with that of the trigone without the suggestion of a *bas-fond.*

On microscopical examination the notable feature was not an increase in the number of acini—which in the normal dog's prostate are as numerous as possible—but a dilatation of the acini. This was quite marked in some portions and very

slight in others; so that in one field one could find normal acini lined by high columnar epithelium (Fig. 3), in others slightly dilated acini lined by low columnar epithelium (Fig. 4), and in others still, large cystic acini lined by flat epithelium (Fig. 5). It was the cystic dilation of the acini which stamped the lesion as true hypertrophy (cf. with Fig. 6 a microphotograph of a section of prostatic hypertrophy in man). There was very marked cellular infiltration of the connective tissue (Fig. 3). Many of these cells were mononuclear, but a few were polymorphonuclear leucocytes. No corpora amylacea were seen.

The *bladder* had a definitely but not markedly thickened wall; otherwise it was quite normal. Trabeculation and *bas-fond* formation were conspicuously absent. The ureters were normal. These characteristics, together with the normally shaped prostatic urethra, made it certain that the hypertrophy in this dog caused no urinary obstruction.

Remarks on the etiology of prostatic hypertrophy.—It is interesting to inquire whether the study of prostatic hypertrophy in dogs would throw any light on the etiology of the condition. There are, as is well known, two rival opinions on the relation of prostatitis to hypertrophy. According to one—recently advocated by Ciechanowski on the basis of extensive, but I think mistaken, pathological observations—prostatic hypertrophy is merely a late stage of inflammation. By the prostatitis the openings of the ducts are blocked, and the so-called hypertrophy is nothing more than a dilation of the glandules behind the obstruction. According to the other opinion—recently urged by Keyes after a study of clinical statistics—prostatic hypertrophy and prostatitis bear no etiological relation to each other. The pathological observations of Hallé, Motz and Albarran are in strong confirmation of this view.

As Geraghty has recently shown in confirmation of the observations by others, urethritis does not occur in the dog. Prostatic hypertrophy, however, does occur. Do not these two facts disprove the inflammatory theory of prostatic hypertrophy? They would, except for the fact that prostatitis, in spite of the absence of urethritis, is of frequent occurrence in the dog. This same phenomenon is observed clinically also in man; in any large genito-urinary practice, cases of definite prostatitis, often with troublesome symptoms, are seen in patients who have neither the history nor the signs of previous urethritis.

Prostatitis, then, occurs without urethritis; and we cannot argue that the absence of urethral inflammation in the dog absolutely disproves the inflammatory theory of prostatic hypertrophy.

On the other hand, the argument of Ciechanowski, that the frequency of acute urethritis and of prostatic hypertrophy in dogs goes to prove their etiological relationship falls, of course, completely to the ground when one knows that what many have regarded as urethritis is really a balano-posthitis, and that a true urethral inflammation in the dogs does not seem to have been demonstrated.

Prostatic atrophy.—In examining dogs in the Hunterian Laboratory to obtain normal prostates for comparison with the hypertrophied gland just described I came across a specimen of prostatic atrophy which is of interest in this connection. The specimen, which is shown in Fig. 1*A*, came from a dog on which double castration had been done three months previously. It consisted of a small bladder, measuring 2 x 2.5 x 1 cm., which was quite normal in appearance. The prostate was, however, only represented by a tiny nubbin of tissue measuring 1 x 0.5 x 0.75 cm. It was separated from the bladder by a neck of the urethra about 0.5 cm. long. The gland, on section, was so small that its gross appearance cannot be described; its cross section was largely occupied by the normal patulous prostatic urethra.

The microscopical examination (see Fig. 7) showed that there had been almost complete substitution of connective tissue for gland tissue. The acini were represented by scattered groups of epithelial cells which had for the most part lost their normal contour and were represented almost entirely by irregular and apparently degenerating nuclei. The lumina of the acini had almost entirely disappeared, though here and there a small space in the centre of a group of epithelial cells represented the remains of a lumen. The richly cellular prostate of the normal dog had become a fibrous prostate.

XIV. THE PARASITES OF BALTIMORE DOGS.

By S. J. Crowe.

The object of this investigation was to determine the varieties of parasites which infect the canine population of Baltimore; to tabulate them, and to note whether any are identical with the parasites known to occur in man. The observations are of value as a preliminary step to the study of the dog's blood, which we hope to take up the following year in the Hunterian Laboratory.

The presence of large numbers of intestinal worms, occasionally of Filaria, and of the great round worm (Dioctophyme Renale) has been observed at autopsies in the various laboratories here for many years. In 1889 Dr. Welch[1] gave a brief description of a number of parasites which he had observed in dogs. Among them was a giant round worm 95 cm. in length. Other specimens have since been seen in various animals, the worms being always free in the peritoneal cavity.

[1] Wm. H. Welch. Animal Parasites. Johns Hopkins Hospital Bulletin, 1890. Vol. I, p. 72.

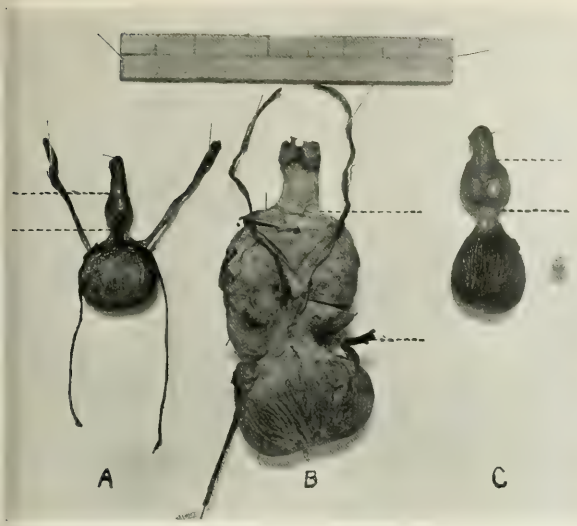

FIG. 1.—*A*. Atrophy of the dog's prostate. Specimen includes bladder, ureters, vasa deferentia, and a portion of the membranous urethra. The dotted lines indicate the anterior and posterior limits of the prostate.

B. Hypertrophy of the dog's prostate. Specimen includes bladder, ureters, and vasa deferentia.

C. The dog's normal prostate and bladder.

The large divisions in the scale at the top of the figure represent inches.

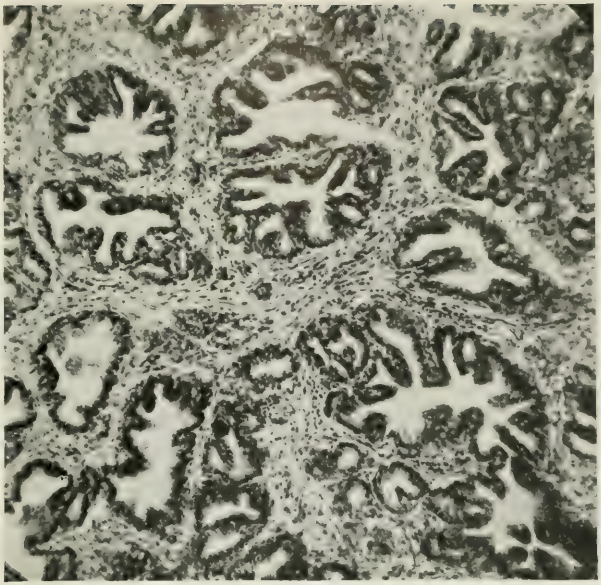

FIG. 2.—Section of normal dog's prostate to show its richness in acini. The picture is the same throughout the gland.

FIG. 3.—Section of hypertrophied prostate in the dog. In this field numerous normal acini are seen. Notice also the marked round-celled infiltration.

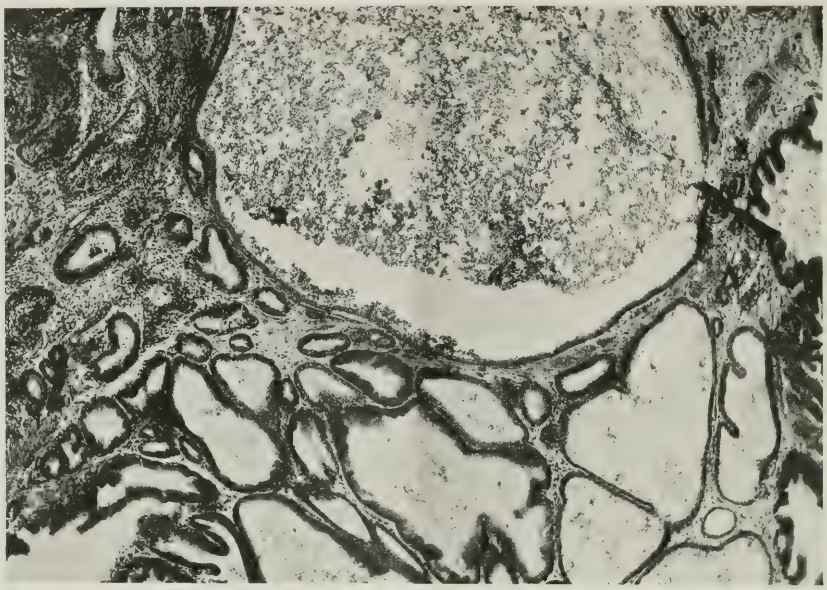

FIG. 5.—Prostatic hypertrophy in the dog, showing marked dilation of the acini.

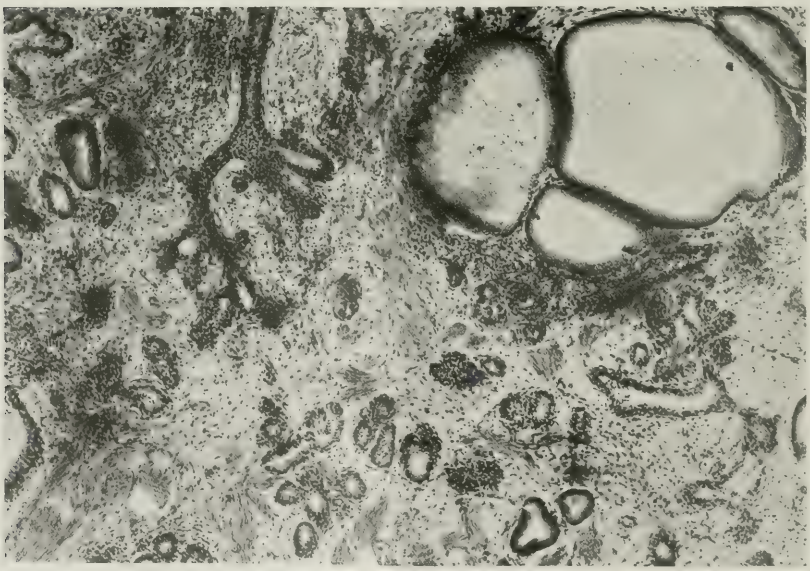

FIG. 4.—Section of hypertrophied prostate in the dog. Normal, moderately enlarged, and greatly dilated acini are seen.

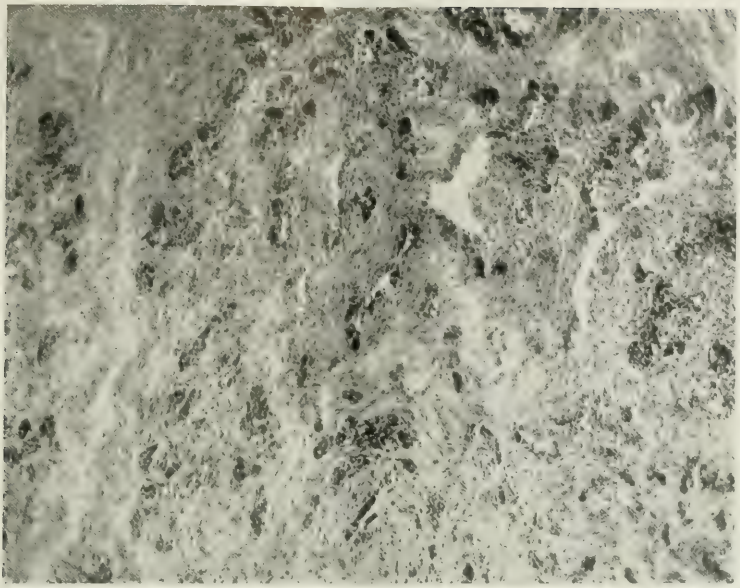

FIG. 7.—Prostatic atrophy in the dog, following double castration.

FIG. 6.—Prostatic hypertrophy in man.

The eosinophilia, due to intestinal parasites, has caused considerable confusion during the course of investigations on the blood of dogs; and since the Hunterian Laboratory has been opened the constant presence at autopsy of some variety of intestinal worm has been especially noticeable. It is in fact extremely common, during intestinal resections, to cut down on a mass of round or flat worms. A number of animals furthermore have died during the first stage of ether anæsthesia, and at the subsequent examination the right heart and pulmonary artery have been found packed with Filaria. Six cases of this sort have recently been reported from this laboratory with autopsy findings.[2]

Methods.—During the past six months post-mortem examinations have been made on 160 dogs. The alimentary tract, from the cardia of the stomach to the anus, was removed and opened. The parasites found were placed in bottles of warm water, the part of the intestine in which they occurred being noted. Smears were made from the gall passages of 39 dogs and examined microscopically, but in no case was there found a liver fluke of any variety. Opisthorcis Pseudo-filineus was especially looked for.

I wish to thank Dr. Charles Wardell Stiles, Chief of the Division of Zoölogy in the Hygienic Laboratory, U. S. Public Health and Marine Hospital Service, for his numerous helpful suggestions, especially in regard to the technique for the preparation and mounting of specimens.

It was found by experience that the flat worms could be stained much better after being fixed between two glass plates, just enough pressure being used to spread the segments out thinly.

The round worms—After being washed:

(1) Place in a hot alcohol solution of corrosive sublimate.

(2) Wash in running water over night.

(3) Place in 70% alcohol with enough iodine to color, more iodine being added as the solution clears up—when it does *not* clear up it means that all the sublimate has been removed.

(4) Put in 95% alcohol (95 parts) plus 5 parts glycerine, and allow to evaporate slowly.

No attempt was made to stain the round worms.

The flat worms—Wash in warm water and allow to macerate in water for 12 hours; or to fix immediately:

(1) Put between two glass plates; clamp them together and immerse the whole in a hot alcohol solution of corrosive sublimate.

(2) Wash in running water over night.

(3) Remove excess of sublimate with iodine plus alcohol if you wish to stain them.

(4) Place in glycerine with plus alcohol and allow to evaporate; alcohol 80-95-70%.

(5) Overstain with acid carmine—decolorize with acid alcohol.

(6) Put in glycerine with plus alcohol to clear.

Parasites found.—From the total of 160 dogs the following seven varieties were found:

(1) *Trichuris depressuscula* (whip-worm) was found in the cæcum of 159 dogs—99.3%.

(2) *Anchylostoma caninum* (hook-worm) was found in the small intestine of 120 dogs—75%.

(3) *Toxacara canis* (common eel-worm) was found in the small intestine of 47 dogs—29.3%.

(4) *Dioctophyme renale* was found only once, free in the peritoneal cavity.

(5) *Filaria immitis* (thread-worm) was found in the right heart and pulmonary arteries of 3 dogs—1.9%. Embryos were found during life in the circulating blood of one animal, of which no post-mortem examination was subsequently obtained.

(6) *Tænia pisiformis* was found in the lower part of the small intestine in 23 dogs—14.4%.

(7) *Dipylidium caninum* was found in the lower part of the small intestine in 112 dogs—70%.

Thus the whip-worm, the hook-worm and the common double-pored tape-worm are almost constantly present in the intestinal tract of dogs.

Trichuris depressuscula (whip-worm) was found in the cæcum of every dog except one; this was a large bulldog, which had never been allowed to run on the streets, but had always been well taken care of and well fed. He died suddenly during an operation on the stomach, and on subsequent examination a round-celled sarcoma was found in the wall of the left ventricle.[3] No parasites of any description were found in his body. The whip-worm of *man* also is one of the most frequent of human parasites, and it is closely related to the species occurring in dogs. All varieties are characterized by the extremely long filiform neck—$\frac{3}{4}$ of the entire body length. The tail, of the male, is curled up, and the spicule protrudes. The eggs are characteristic—oval in shape, with plugs in both ends. An intermediate host is not necessary for their development and dogs constantly reinoculate themselves. The eggs, after being discharged in the fæces, undergo development, and with the contained embryo are swallowed in water or food.

Neither in man nor in animals does it seem to give rise to any symptoms. Guiart, of Paris, has recently advanced the view that whip-worms form the portal of entry for typhoid bacilli. The examinations made in Washington, D. C., by Dr. Stiles, of 200 typhoid patients failed to bear this out, however. Dr. Kelly, in his book on Diseases of the Appendix, says: "There is undoubtedly an etiologic relation between appendicitis and some forms of intestinal parasites . . . . In several instances children with symptoms of appendicitis have been entirely relieved by santonin. Metchnikoff (Semaine méd., 1901, No. II) justly lays stress upon the necessity of microscopical examination of the stools for ova in all cases in which there is any room for suspicion, a measure especially important in children. The rôle of the worms may be to produce an erosion of the mucosa, and so open the way for the invasion of bacteria."[4]

Sections through the walls of the cæcum of dogs show that

[2] Six Cases of Infection with Filaria Immitis. J. G. Hopkins. Johns Hopkins Hospital Bulletin, Vol. XVII, December, 1906, p. 377.

[3] Bryant. Cf. No. XVII of these reports.

[4] Kelly-Hurdon: Vermiform Appendix and its Diseases.

the whip-worm does burrow into the mucosa to a slight extent, but excites no inflammatory reaction whatever.

Ancylostoma caninum (hook-worm).—The species occurring in dogs is not identical, but closely related to the Uncinaria of man.[5] They have a heavy armature of sharp teeth, and the head is often found imbedded in the mucosa, and surrounded by a small extravasation of blood. Frequently eight or ten are seen together within an area the size of a quarter, which is injected and considerably thickened (probably due to secondary bacterial infection). The hæmorrhagic enteritis, which is frequently seen in dogs, especially after an operation, is *associated* in many instances with a heavy *hook-worm* infection. In two such cases of bloody diarrhea last year an infection with Coccidium Bigeminum was found (Bancroft-Cross, Johns Hopkins Hospital Bulletin, 1906, No. 189). Positive evidence that the hook-worm was the cause of anæmia in these animals could not be found. The life cycle and mode of infection is probably much like that for the Uncinaria of man—that is, the eggs escape in the fæces and rapidly develop in the presence of moisture.

Infection of man takes place in two ways:

(1) The larvæ penetrate the skin, reach the circulatory system, pass through the heart to the lungs, from the lungs to the air passages, up to the larynx, down the esophagus to the stomach and to the small intestine, where they develop into adults. Looss has experimentally demonstrated that this is a common mode of infection. *Ground-itch* is supposed to be the initial lesion in man, but although carefully looked for, no such lesions could be demonstrated in the infected dogs.

(2) A second mode of infection is through the mouth, with contaminated food and water.

Toxacara canis (Fig. 8).—This is the common eel-worm of dogs and cats. It is easily recognized by its arrow-shaped head. Eight cases have been reported in man—in most of these the worms were vomited. They were found in 47 of the dogs examined. In one, a bulldog, there were about 200 individuals, most plentiful in the upper duodenum, but in relatively large numbers as far down as the cæcum. It looked as if they must certainly have caused an intestinal obstruction. The common dog tape-worm (Dipylidium Caninum) is almost invariably entangled with them. Just as with Ascaris Lumbricoides of man, the development is without an intermediate host. The eggs escape in the fæces, and slowly develop into embryos. If these are swallowed with contaminated food, water, or from dirty hands, the embryos develop directly into the adult, which explains the varying size of the worms found in the intestines. The infected dogs seem to show no symptoms, although occasionally the worms are passed in large numbers. Dr. Stiles has found the eggs in the intestines of the common house fly.

Dioctophyme renale (Eustronogylos Gigas) (Fig. 9).—This is one of the largest round worms known. It was found once in this series. It occurred in a small male fox-terrier. He was rather emaciated, but had otherwise shown no symptoms. In the literature it is described as occurring most frequently in the kidney, but in this instance it was found lying free in the abdominal cavity.[6] The kidneys were grossly and microscopically normal in appearance, and there was no free fluid, or demonstrable lesion of the peritoneum. This specimen was 74 cm. in length, and of a bright red color with black stripes running longitudinally. It felt soft and fluctuating, much like a soft rubber tube filled with water. It is said to occur in the kidney of dogs and various other animals; and about a dozen cases have been reported in man. But in the laboratories here it has invariably been found free in the peritoneal cavity. At a meeting of the Johns Hopkins Medical Society in March, 1890, Dr. Welch showed a specimen of this worm, 95 cm. in length. It was found free in the peritoneal cavity, and he mentions that it has been found three times previously in dogs used for experimental work. The source of infection is not known.

Filaria immitis.—Four dogs were found to be infected with this parasite. Two of the dogs died during an ether anæsthesia; a third took ether well and recovered from a gastrostomy. He was finally sacrificed and at autopsy the cavity of the right ventricle contained a mass of long, white, thread-like worms, varying from 10 to 25 cm. in length (Fig. 10). They extended out into the pulmonary arteries of both lungs, apparently blocking the lumen almost entirely, and interfering with the action of the pulmonary valves to a considerable extent. One worm was found in the inferior vena cava between the liver and heart.

Mosquitoes, anopheles and culex form the intermediate host.

There is no well authenticated case of infection of man by this parasite.

Tænia pisiformis.—This is a tape-worm which dogs contract by eating rabbits infected with Cysticercus Pisiformis. It was found in the lower portion of the small intestine in 23 of the dogs examined. Vital, in 1874, reported the occurrence of this tape-worm in man, but the correctness of the zoölogical determination is doubtful; especially since Galli-Valeria, in 1898, was unable to inoculate himself by swallowing the larval stage. It can be easily produced in dogs by feeding a rabbit's liver containing the cysticercus forms.

The adult varies in length from two to four feet; the head is surmounted by a short, thick rostellum, which has a double row of hooks. The genital pores open laterally, irregularly alternate, and are very prominent.

[5] Stiles. Osler's Modern Medicine, Vol. I, 1907. U. Americana causes in man: tunnel disease, miner's anæmia, brickmaker's anæmia, etc.

U. Stenocephala occurs in dogs, foxes, etc., and causes considerable trouble in the blue fox industry.

U. Trigonocephala occurs in sheep and produces a serious anæmia. In Victoria and Calhoun Counties, Texas (in conjunction with the twisted wire-worm—Hæmonchus Contortius), it causes the death of 25% to 59% of certain flocks.

U. Lucosci in seal pups (Alaska). It is responsible for about 17% of deaths of the pups.

None of the species from animals are known to infect man.

[6] Since this writing a second case of infection with this worm has occurred among the laboratory animals.

FIG. 8.– Toxacara Canis; from small intestine of dog.

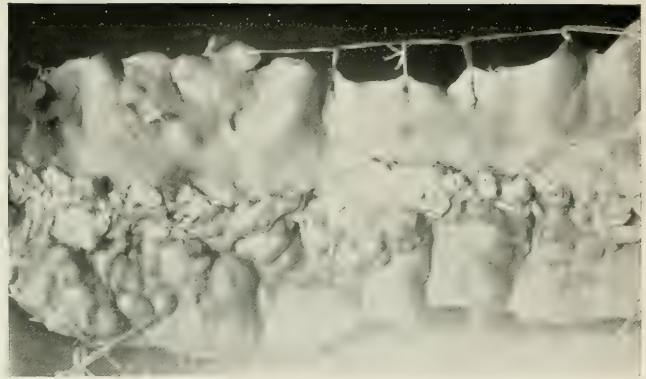

FIG. 12.—Œsophagostoma Columbanum; encysted embryo in the intestine of the sheep.

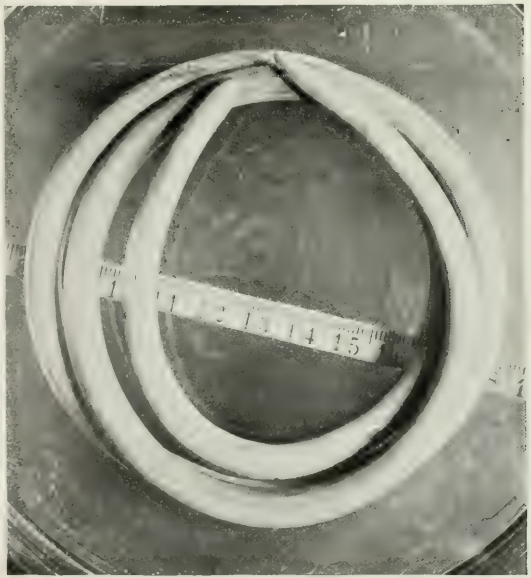

FIG. 9.—Dioctophyme Renale; from peritoneal cavity of dog.

FIG. 10.—Filaria Immitis; showing presence of the parasites in the right ventricle and pulmonary arteries.

FIG. 11.—Dipylidum Caninum; from the small intestine of the dog.

Dipylidium caninum (Fig. 11).—This is by far the most common tape-worm found in dogs. It is small—from 10 to 30 cm. in length, and is easily recognized by its double set of reproductive organs, with the genital pores opening laterally on both sides. The head is small and has a conical rostellum which is armed with several rows of very minute hooks. The parasite has very little, if any, effect on its animal host. The larval stage lives in the lice and fleas of dogs, and in the human flea. These insects become infected with the larvæ while they are gnawing at the matter attached to the hairs of the dog. In trying to rid himself of the fleas the dog swallows some of the larvæ and so becomes infected.

Other parasites.—In addition to the dogs, a few rabbits and a goat were examined.

Coccidium oviforme.—The livers of two rabbits were found studded with small, yellowish patches, and on microscopical examination numerous characteristic oval bodies were seen. The cysts were seen to be dilated gall-ducts, lined with columnar epithelium, which projected, as folds, into the lumen. Lying free in the cavity and embedded in the epithelium were thousands of the small, oval bodies.

Several cases of infection of man with the Coccidium Oviforme have been reported, the liver, kidneys and intestines being most frequently affected.[7]

Œsophagostoma columbanum (Fig. 12).—One sheep, which had been used for parathyroid experiments, was autopsied. On opening the peritoneal cavity numerous prominent nodules were seen in the wall of the large intestine, varying in size from 3 cm. to 0.5 cm. in diameter. On section they were firm and filled with a greenish, cheesy mass. Under the dissecting microscope a small embryo-worm could be gotten out, which was just visible to the naked eye. The adult worms, which are about the same size and closely related to the hookworm, were found in the lumen of the intestine.

The life cycle outside the sheep is not known; the youngest known forms are those encysted in the walls of the intestine. After several months they leave the cysts and begin adult life in the intestine. They seem to cause but little trouble, but in some cases general debility and diarrhea are associated with their presence.

[7] Leukart: Parasiten des Menschen.

Among the other parasites which occur in both man and dog are:

(1) *Dibothriocephalus latus.*—The large, broad tape-worm which varies from 15 to 30 feet in length. The larval stage is found in the muscles and organs of fresh water fish. "The special medical significance of an infection with the broad tape-worm is the tendency to develop a severe anæmia, resembling pernicious anæmia, and supposed to be due to a toxin." The red blood count may be as low as 1,300,000.

(2) *Ecchinococcus.*—This is one of the smallest tape-worms known. Cases of infection occur most frequently in Iceland, and most of the cases in the United States occur in immigrants who were probably infected before they came to this country. The adult worm occupies the upper half of the small intestine, but never close to the stomach. The larval stage occurs in hogs, sheep, cattle, etc. Man is probably an accidental host. The eggs are discharged in the dog's fæces, become matted in his hair, and man is probably infected from hands soiled while petting dogs. "Iceland is recognized as the classical Ecchinococcus land—the most conservative statistics give the infection as from 1 in 43 to 1 in 63 of the inhabitants. Krabbe reports it for 25 per cent of the dogs."[8]

No case of infection was found in these dogs, although smears from the duodenum of 50 dogs were examined microscopically.

As regards prevention, Dr. Stiles says: "Since this disease is transmitted from dogs to man, and since dogs obtain their infection more particularly from eating the infected organs of slaughtered sheep, cattle and hogs, it is clear that any plan of prevention must follow two lines:

(1) Dogs should be kept away from slaughter houses . . . . ; and the rule that no dog which enters a slaughter house or its refuse yard should ever be allowed to leave would, if carried out, save many lives and much valuable stock.

(2) All stray dogs should be killed—the dog pound is an institution of practical hygienic importance."

Neither of these parasites were found in this series of dogs, but the possibility of their occurrence should always be borne in mind.

[8] Stiles in Osler's Modern Medicine, Vol. I, 1907.

XV. OSTEO-SARCOMA OF THE RADIUS IN A DOG.

By F. F. GUNDRUM.

History.—The patient, "Caesar," a thoroughbred Great Dane, after some correspondence in regard to his condition, was admitted to the clinic on January 15, 1907. His owner gave the following account of his malady:

The dog is five years of age. He has always been an active and spirited animal, and a prize-winner at several bench shows. About one year ago (January, 1906) a small enlargement appeared on the right foreleg just above the wrist joint. Though firmly attached to the bone, this growth did not seem to be painful or tender and was not adherent to the skin. The swelling slowly increased in size (Fig. 13) until in October, 1906, when it was incised by a veterinarian, under the impression that it was a "bone abscess." No pus was found, but the incision caused a profuse hæmorrhage, which was controlled with difficulty. The wound has never healed and the swelling has continued to enlarge.

In November, 1906, an X-ray photograph (Fig. 14) was taken, which showed a large tumor arising from the shaft of the radius. About a month later, December, 1906, what seems to have been a

pathological or spontaneous fracture occurred, accompanied by rather free bleeding from the granulating wound. During the past six weeks the tumor has grown rapidly and the whole leg has become very much swollen. The animal has not used the leg in walking since the fracture took place, due apparently to the fact that it will not support his great weight, rather than to any pain which the effort occasions.

Examination.—The animal is a beautiful example of his species, standing 2 feet 10 inches in height at the shoulder, and weighing 160 pounds. Aside from the local lesion the physical condition reveals no abnormalities.

Just above the wrist-joint of the right fore leg there is a hard, roundish enlargement, which greatly deforms the thin shaft of the limb. The tumor is about 35 cm. in circumference and has evidently arisen from the bone—the radius alone being involved, as shown by the X-ray. On the front of the tumor (Fig. 15) there is a sharply outlined ulcerated area, 7 x 5 cm. in its surface dimensions and 1.5 cm. in depth. The ulcer has a necrotic base and discharges a thin, foul-smelling fluid. On palpation the tumor is of stony hardness, except at the base of the ulcer, which is spongy and bleeds easily. The skin overlying the tumor is œdematous and seems to be firmly attached to the growth. Though the entire leg from shoulder to toes is swollen to nearly double the size of the opposite leg, the foot is particularly œdematous. A large, firm gland can be felt in the posterior axillary fold. On manipulation of the paw, crepitus is easily elicited, owing doubtless to a pathological fracture. There is no especial tenderness and the animal does not hesitate to put the paw to the ground in walking, though he spares it by limping.

A diagnosis of osteo-sarcoma in this case was easily made, and although the histological character of the tumor was not certain it was thought to be of the spindle-celled variety—a form which in man is attended with a grave prognosis. The ulceration of the growth, furthermore, added to the seriousness of the condition. It was impossible to tell whether the palpable glands were enlarged through inflammatory hyperplasia or metastatic involvement.

As the animal, aside from being a great pet, was particularly valuable for breeding purposes, it was determined, at the owner's solicitation, to attempt an amputation at the elbow-joint in the hope of prolonging his life and usefulness.

Operation.—After a preliminary injection of morphia the patient was placed on the table, the ulcerated wound was disinfected and the entire extremity shaved and prepared before the administration of ether. A racquet-shaped incision was made through the skin about the elbow-joint and the flap turned back. The tissues were found to be boggy and the cutaneous veins unusually large and numerous. As the dissection was carried down to the main vessels of the limb on the inner side of the humerus the operator encountered a dense, white cord of tissue, completely surrounding the brachial artery and vein. This solid cord, in which the brachial vessels were embedded, was presumed to be a lymphatic extension of the new growth upward from the tumor. The operation consequently was abandoned at this point in favor of a higher amputation. A new incision was made about the shoulder, where the leg was almost as large as a child's thigh, and after a long dissection, when the axillary vessels were exposed it was found that the same cord of new tissue ran in a continuous line from the tumor to the very apex of the axilla and to the wall of the thorax. Deeming the case a hopeless one, from the certainty of early recurrence, probably in the operative wound itself, the dog was not allowed to recover from the anæsthetic.

Autopsy. The abdominal and thoracic organs were found to be practically normal. There were a few vegetations on the mitral valve, due to an old endocarditis. There were no signs of internal metastases.

Tumor. On gross examination it was seen on section of the tumor (Fig. 16) that it consisted of two quite distinct forms of tissue; a central portion, soft, red, spongy, and containing several spicules of bone, and a peripheral portion showing a firm, dense, whitish growth, resembling in its appearance the cord of tissue which, at the time of operation, was found to extend along the vessels upward into the axilla. Four enlarged glands were found at autopsy, one near the elbow and three in the neighborhood of the axilla. All showed firm, white areas which from their macroscopic appearance were considered to be metastases.

From the gross appearance a pathological diagnosis was made of sarcoma of the radius with extension to the lymph vessels of the leg and to the axillary glands.

On microscopic examination of the tissues the soft, central part of the tumor proved to be a spindle-celled sarcoma which contained, in addition, a number of giant cells. There was a scanty fibrous tissue framework. The dense, white surrounding growth, which had extended to the lymphatics, consisted of a rather œdematous fibrous connective tissue, very rich in blood-vessels, but on sections taken from near the tumor, the elbow, and the shoulder, no typical spindle cells resembling the original tumor were seen. All the lymph glands showed sinuses crowded with large phagocytic cells, many of which contained modified blood pigment. In every gland were evidences of endothelial hyperplasia, but in none were definite metastases or any spindle cells seen. The microscopical diagnosis was spindle-celled sarcoma with giant cells, fibroid induration around the tumor and great vessels, and endothelial hyperplasia of the lymph glands.

Discussion.

Most authorities agree that sarcoma is a less common tumor in dogs than carcinoma, and this corresponds with our experiences at the Hunterian Laboratory. During the past three years, although there have been a number of mixed tumors, we have seen only five other instances of primary sarcoma; one in an undescended testis (4), one in the heart wall, the third a periosteal sarcoma of the head of the humerus, the fourth a melanotic sarcoma of the scrotum, and the fifth a fibro-sarcoma of the neck with hepatic metastases.

Cadiot (1) states that bone sarcomata occur in dogs of all ages and species, but these tumors seem especially liable to appear in animals which have been kept in confinement and have lived on a meat diet. Further, bone sarcomata are rare and nearly always recur after operation, so that the prognosis is very unfavorable.

Hobday (2) also emphasizes the hopeless outlook in sarcomatous tumors of bones.

On the other hand French (3) draws a sharp distinction in regard to the prognosis between the periosteal and medullary varieties and considers the latter to be relatively benign, especially since they are tardy in giving metastases. Sarcomata, according to this same author, are especially likely to occur about the head, sternum, and the ends of the long bones. Early lameness is an extremely important symptom in sarcoma of the long bones, for it is very suggestive of a medullary growth.

As in the case we have recorded, the failure to recognize the true nature of these tumors at an early date and to give them the benefit of surgical treatment makes statistics very meager and, from an operative standpoint, quite unreliable.

FIG. 13.—Photograph of patient taken in October, 1906, showing appearance of tumor before exploratory incision was made.

FIG. 14.—Radiograph of osteo-sarcoma of the radius.

FIG. 15.—Photograph of tumor before operation, showing ulcerated area; ightly reduced.

FIG. 16.—Section through the centre of the growth; reduced one-third.

A great majority of the animals thus afflicted are sacrificed without attempting a surgical cure.

An early amputation in our patient would doubtless have saved his life, and it is quite possible that this might have been accomplished even at the late date it was attempted had we not depended on the macroscopic appearance alone of the cord of tissue met with at the operation, supposing it to be an extension of the disease. The nature of the primary growth was recognized before the amputation was undertaken, but it was hoped that the tumor had remained a local one. Although sarcomata usually spread by way of the blood-vessels, the direct continuity with the original neoplasm of the ascending column of solid new tissue made it seem unlikely that a mere lymphatic hyperplasia could account for the condition observed. The failure to find any tumor cells in the microscopical examination of the tissues taken from three or four different levels, does not exclude the possibility of there having been metastases in other areas of the fibrous growth, but it demonstrates at least that not all of the new formation was sarcomatous in origin. Sections also were made from all of the enlarged glands, and in them likewise it is probable that the abnormality seen in the gross was due to the action of toxines and phagocytic cells in the lymphatics which drained the infected and ulcerating growth below.

The spindle-celled sarcomata with giant cells are, in man, of comparatively low malignancy, and, although there are no very definite data on the subject it does not seem improbable that the same may be true in a general way in dogs. The course of this case seems rather to point toward that conclusion. The experience with this patient, therefore, shows how misleading the gross appearances of a column tissue involved in chronic lymphangitis may be, and shows furthermore that an attempt to save life under similar circumstances in the future may be justifiable. Our previous experience with amputations—even those of the interscapulo-thoracic form and in large animals—has taught us that mutilating operations of this kind leave the animal almost as active and as well able to care for himself as when the possessor of four legs.

The literature on bone sarcoma in dogs is not very extensive and no attempt has been made to give all the references. Probably the most satisfactory discussion is to be found in French's recent work.

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XVI. ON THE ALTERATIONS IN BODY TEMPERATURE PRODUCED IN DOGS BY MORPHIA AND ETHER.

By Charles Wilson Mills.

These observations comprise data secured in four different ways.

First.—A compilation of the temperature curves of animals taken during operations in the regular third year course of operative surgery. All of these dogs were anæsthetized with ether, after a preliminary injection of morphia.

Second.—Observations to determine the effect on temperature of morphia alone.

Third.—Observations to determine the effect on temperature of ether alone.

Fourth.—Observations to determine how greatly the morphia and ether temperature curves may be influenced by the application of external heat.

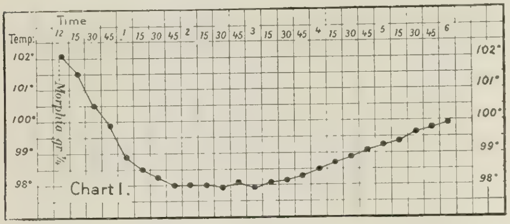
Though this was the sequence in which the observations were made they seem more logically to fall into the following order: First, the effect of morphia alone; second, the effect of ether alone; third, the effect of morphia and ether, no unusual precaution being taken to preserve body heat; fourth, the effect of morphia and ether when such precautions were taken. The figures record the rectal temperatures.

Group I. Showing the effect of morphia alone.—Records of three dogs, after the administration of ¼ grain morphia hypodermically. Animals in usual position on operating tables without covering:

	Before morphia.	½ hr. after.	1 hr.	1½ hr.	2 hr.	3 hr.	4 hr.	5 hr.	6 hr.
1.	101.0°	99.0°	98.4°	98.6°	98°	97.6°	98.6°	98.8°	99.2°
2.	102.0°	101.2°	99.6°	99.2°	99°	99.2°	99.8°	100.6°	101.2°
3.	103.1°	101.2°	98.5°	97.6°	97°	97.0°	97.6°	98.6°	99.4°
Average	102.1°	100.5°	98.8°	98.3°	98°	97.9°	98.5°	99.3°	99.9°

The curve on following page was plotted from the averages of the figures, taken in these three cases at 15-minute intervals

These figures indicate that morphia alone, in dogs, unprotected by covering or by external heat, produces a fall in temperature with a curve showing the following characteristics: *First,* a steady fall for 1½ to 2 hours, amounting to from 3° to 5° drop below normal. *Second,* the temperature then

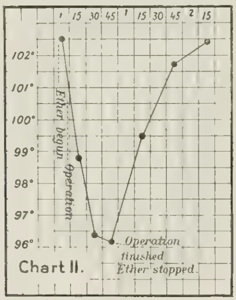


remains constant at this lowest level for about 2 hours. *Third,* at end of this second period, or in from 3½ to 4 hours from the administration of the drug, the temperature begins gradually to rise again, the rise being so slow that at the end of six hours it is still from 1° to 3° below normal. During this period the dogs are gradually recovering from the effects of the morphia.

Group II. Showing the effect of ether alone.—Records of six dogs. Operation, laparotomy. Moderately cold room and dogs not protected. Ether administered during operation for about 45 minutes in every case:

	Before ether.	15 min. after.	30 min.	45 min.	1¼ hr.	1¾ hr.	2¼ hr.
1.	102.4°	99.6°	96.4°	98.2°	100.4°	100.4°	102.4°
2.	102.6°	98.0°	95.6°	95.2°	98.5°	101.6°	....
3.	102.2°	98.2°	96.4°	95.6°	...	....	....
4.	102.0°	100.0°	97.8°	96.6°	...	....	....
5.	102.8°	98.0°	96.0°	96.6°	99.6°	101.6°	....
6.	103.0°	98.4°	95.6°	94.6°	...	....	....
Average	102.5°	98.7°	96.3°	96.1°	99.5°	101.2°	102.4°

The curve plotted from these averages is shown below:



These figures show that ether alone causes a fall in temperature in unprotected dogs. The fall in these cases was about 6° during the first half hour, but the coldness of the room makes this fall much greater than would have taken place under ordinary operating-room conditions. On discontinuance of ether the temperature rapidly rose, reaching normal in about 1½ hours, at which time the dogs had recovered from the anæsthetic.

Group III. Showing the effect of the combination of morphia and ether.—Records of 26 dogs, all operated on. Morphia, ¼ grain, administered 2 hours before beginning the administration of ether. Three of these animals were sacrificed, and 23 were allowed to recover from the anæsthetic. The lowest temperature during the course of the various procedures varied from 98.4° to less than 94°. The amount of the fall, however, seemed to have no definite relation to the operative recovery, although there was no mortality among the animals whose temperature did not drop below 98°, whereas 50 per cent of the small number with a fall to 94° subsequently succumbed. The matter probably bears some relation to pulmonary complications.

The size, sex and breed of the dog were noted on some of the records, and it would seem that the prognosis is better for large than for small animals, and better for males than for females.

With the exception of three major amputations the operations were all abdominal sections. The drop in temperature was fully as pronounced in the former as in the latter, the lowest temperature in the three amputated dogs being 94.5°, 95.5°, and 94.5° as against an average of 96.3° for the whole series. The fall in temperature, therefore, apparently does not depend on the exposure of the abdominal cavity and cooling of the viscera.

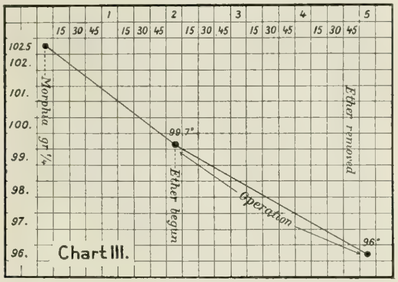
The temperature records of this set of dogs show in every case a fall of temperature following the administration of ether. In many of the dogs this fall was later followed by a rise. The records have accordingly been divided into two classes: (1) those showing a continuous drop during operation, and (2) those showing a preliminary drop followed by a rise.

Class I.—Records of 14 dogs showing a continuous drop during operation. Length of operation from 1½ to 4 hours. Operations included 11 laparotomies and 3 amputations:

	Temp. before ether.	Temp. at end of operation.	Length of operation.
1.	97.4°	94.0°	4 hours.
2.	98.4°	96.4°	3¼ "
3.	101.0°	94.0°	4 "
4.	96.0°	94.5°	1½ "
5.	103.0°	97.0°	2 "
6.	102.8°	94.0°	2¾ "
7.	101.2°	96.2°	3 "
8.	98.4°	95.0°	3½ "
9.	100.0°	94.5°	4 "
10.	100.2°	95.5°	3¼ "
11.	100.0°	94.5°	2 "
12.	100.5°	96.0°	2¾ "
13.	98.5°	94.5°	3¼ "
14.	98.0°	95.8°	2½ "
Average	99.7°	96.0°	3 "

Regarding the dog's normal temperature as 102.5°, the curve plotted for this class will be as shown in Chart III.

Comparing this curve with the curve obtained from morphia alone (Chart I), it will be seen that ether, administered at the lowest point of morphia curve, causes an additional fall in temperature. The morphia curve has reached its lowest point at the end of two hours, while ether given at this time produces a still further drop, averaging 3.7°.

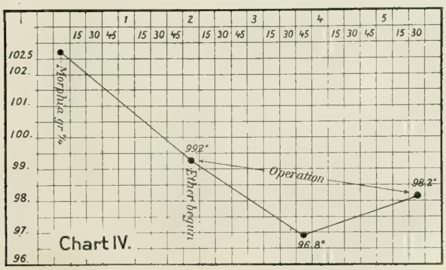


It is probable that these dogs did not all receive a full quarter grain of morphia, so the average fall produced by the morphia at the end of two hours is not quite as great as in the previous record—99.7° as against 98°.

Class II.—Records of 12 dogs, showing a drop after administration of ether followed by a rise to end of operation. Length of operations, from 3 to 5 hours, all laparotomies:

	Temp. before ether.	Lowest temp.	Length of falling period.	Temp. at end of operation.	Length of operation.	Point in operation at which rise began.
1.	101.0°	97.7°	2¼ hrs.	100.0°	3½ hrs.	Suturing stomach.
2.	97.4°	94.6°	1¾ "	96.6°	3½ "	Incision into stom.
3.	101.0°	97.8°	1½ "	100.8°	3½ "	Incision into peritoneum.
4.	98.2°	94.6°	1 "	96.2°	3 "	Incision into intestine.
5.	99.0°	97.0°	2 "	98.6°	3¼ "	....
6.	99.0°	98.0°	1 "	100.6°	3¼ "	Incision into stom.
7.	99.6°	95.7°	2 "	97.0°	3¾ "	....
8.	98.0°	95.6°	2¼ "	96.6°	3 "	....
9.	100.8°	96.2°	1¾ "	96.6°	2¼ "	Closure.
10.	96.5°	95.0°	1½ "	95.5°	2¼ "	....
11.	101.4°	97.2°	4½ "	97.4°	5 "	Closure.
12.	100.0°	98.4°	1 "	100.6°	5 "	Incision into stom.
Av.	99.2°	96.8°	1¾ "	98.2°	3½ "	

The curve obtained from these averages is as follows:



These figures show a drop after the ether is begun, just as in Class I. In from 1 to 2 hours, however, after the beginning of the ether, or from 3 to 4 hours after the morphia, the temperature begins to rise, this rise in some cases amounting to 3° above the lowest temperature, and averaging in all the cases 1.4° at the end of operation.

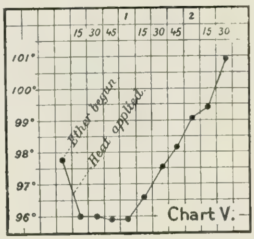
In attempting to explain this phenomenon the point in the operation which had been reached when the rise began was first considered, but as can be seen from the preceding table, these probably bear no relation to each other, since the rise may begin at any stage of the operation from the opening of the peritoneal cavity to the final closure.

The rise seems on the other hand to bear a definite time relation to the beginning of the ether, occurring between 1 and 2¼ hours after this in every case (except one, 4½ hours, for which a different explanation must probably be sought). As the morphia was given 2 hours before ether, the rise begins in from 3 to 4¼ hours after the morphia, or 3¾ hours on an average. Referring now to the morphia chart (Chart I) it will be seen that the morphia curve begins to rise between 3 and 4 hours after the administration of the drug, closely corresponding therefore to the time of the rise in the dogs under consideration.

The explanation, therefore, for this rise of temperature during the operation is probably to be found in the wearing off of the effect of the morphia.

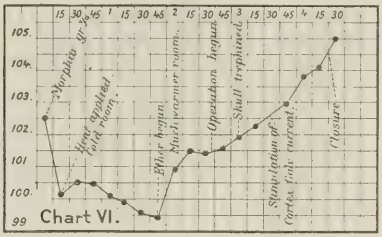
A comparison of the mortality figures of the 14 dogs in Class I and the 12 dogs in Class II shows that there were more fatalities among the former than among the latter. This would indicate that there is a better operative prognosis among animals, anæsthetized in this way, when this late rise in temperature occurs during the operation than when it does not.

Group IV. Showing the effect of morphia and ether, when the patient is protected by external heat and by coverings.—Having determined the nature of the temperature curve of animals under the influence of morphia and ether, the attempt was made to see how much this curve could be modified by applying external heat to the dogs while under the influence of the anæsthetics. The curves of two dogs, obtained under these conditions, are given. The heat was supplied from an electric heating-pad placed under the patients, and they were further protected by blankets.



Dog No. 1. (Chart V)—Operation, tracheotomy and thoracotomy with resection of rib. The heat was not applied in

this case till after the ether had been begun. The heat apparently had little effect for ¾ of an hour, after which the temperature began to rise, and an hour and a half later was 101°, a much greater temperature than that obtained at a similar stage from any of the unprotected dogs.



Dog No. 2. (Chart VI)—Operation, craniotomy and galvanic stimulation of motor area of cortex. The heat in this case was applied soon after the administration of morphia. The dog at first was in a cold room and the heat rather imperfectly applied. Under these conditions the body temperature still continued to fall, reaching 99.5° in 1¾ hours. At this time the dog was removed to the operating room, which was much warmer and where the heat could be more perfectly applied. The temperature at once began to rise in spite of the administration of ether, and steadily advanced to 105° in 3 hours, at the end of operation, or 2.5° above the dog's normal. In this experiment the stimulation of the cortex may possibly have had some effect through disturbance of the thermic centres, although the marked and abnormal rise is probably mainly due to the high surrounding temperature.

Conclusions.

I. The dog's normal temperature is between 102° and 103°.

II. Morphia, ¼ grain, at ordinary room temperature, causes a drop of from 3° to 5°, reaching lowest point in 1½ to 2 hours, remaining steady there for 2 hours more, and then gradually rising as the effects of the drug wear away.

III. Ether alone causes a fall in temperature, its extent depending largely on the surrounding temperature, remaining down during the administration of the drug, and rapidly rising to normal on its discontinuance.

IV. Morphia and ether in combination cause a greater drop in temperature than morphia alone, the average fall amounting to 6° in dogs under ordinary operating-room conditions.

V. The rise of temperature due to the wearing off of the effects of morphia may take place despite the fact that the dog is simultaneously under the influence of ether anæsthesia, or, on the other hand, the effects of the ether may be so great that no rise occurs.

VI. If heat be applied externally to dogs under morphia or ether the fall in temperature is much less, and if the heat be continued long enough, the temperature rises to normal or even above normal levels.

VI. Prognosis. In the dogs operated on under the conditions mentioned the prognosis seems better in large than in small animals, in males than in females, and in dogs showing a rise in temperature as the effect of morphia wears off. The amount of fall of temperature apparently does not affect the prognosis.

VII. The nature of the operation seems to have no definite bearing on the temperature curve.

XVII. A STUDY OF REVERSAL OF THE INTESTINE.

By R. D. McClure and H. F. Derge.

Normal peristalsis passes downward away from the stomach. Peristalsis may pass toward the stomach in certain abnormal conditions, as in isolated pieces of intestine or in the exposed intestine of living animals. Antiperistalsis, as has been pointed out by Cannon, normally occurs in the ascending colon, and these waves are even more frequent here than those normally directed.

The fact that reversal of peristalsis occurs after an obstruction and after stasis of the intestinal contents suggests that reversal of the peristalsis might entirely and permanently replace the normally directed peristaltic waves, if the exciting cause of this abnormality be maintained for a sufficiently long time, and still be compatible with the life of the individual.

Since the original investigations of Mall (1) and Halsted in 1887 many studies of intestinal reversal have been made, the results being largely confirmatory of those first obtained. In these early observations the animals rarely lived more than one or two months before showing symptoms of emaciation and intestinal obstruction. Mall found that the mucous membrane of the dilated portion of the bowel at the upper end of the loop was converted into fibrous tissue and that the muscular layers were much hypertrophied above the upper suture; also that the vessels passing to the reversed loop were all greatly widened and elongated, showing that the intestinal dilatation was accompanied by hypertrophy of all parts of the bowel and was not a simple mechanical distention. His observations led him to believe that under normal circumstances the vermicular action is always in one direction and away from the stomach. The accompanying photographs (Figs. 17, 18) from two of our cases show the gross appearances of the spindle-shaped enlargement which occurs about the proximal suture.

Kirstein (2) (1889) explained the dilatation at the upper end of the reversed loop by the meeting of the downwardly directed stream of the normal intestine and the upwardly directed one of the reversed loop. Nevertheless he was of the opinion that an antiperistaltic movement had taken place.

FIG. 17.—Showing reversed loop in situ, to give an idea of the relative enlargement of the distended and hypertrophied portion of the bowel. Proximal line of suture at *A*.

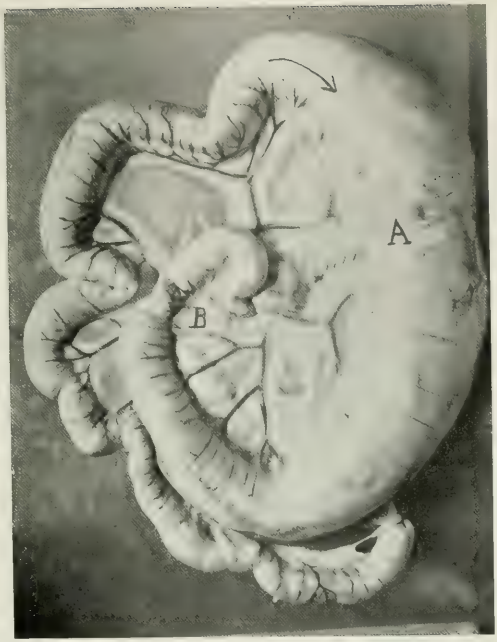


FIG. 18.—Showing enormous spindle-shaped dilatation on either side of the upper anastomosis, *A*. The point of greatest dilatation is 3 cm. above the suture on the normally directed intestine. Lower anastomosis of reversed loop at *B*, where lumen remains of normal size.

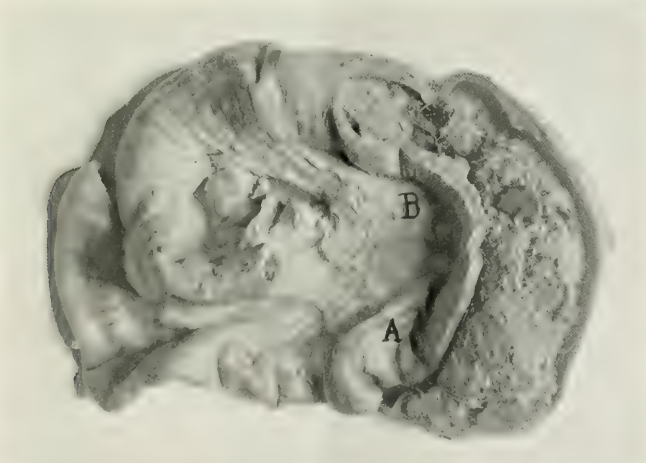


FIG. 19.—Showing character of impacted contents. Note great thickening of intestinal walls on section.
A. Proximal line of suture.
B. Distal line of suture.

Edmunds and Ballance (3) (1896) found that the reversed loop becomes considerably shorter.

Kauders (4) (1892) obtained the same general results with cats; but he found atrophy of the gastric and intestinal mucosa and a sac-like dilatation. While Mall's and Kirstein's observations agreed in attributing the dilatation to the pressure of the opposing peristaltic streams, Kauders attributed it to atony of the reversed gut.

Kelling (5) (1900) reported a case of reversal with apparently normal health sixteen months after the operation, and concluded that antiperistalsis had taken the place of the normal peristalsis.

Mühsam (6) (1900) reversed the entire jejunum and ileum. Although there were no survivals after this extensive reversal his observations led him to believe that antiperistalsis took place.

Enderlen (7) (1901) used the lateral anastomoses in his experiments instead of the end-to-end method. He performed a series of metabolism experiments and found that the food underwent normal combustion in the intestine. He believes that the vis à tergo does not entirely explain the passage of intestinal contents through the loop, but that there is also antiperistalsis.

In our series of experiments portions of the intestine varying in length from 12 to 75 cm. were reversed. The Connell method of end-to-end anastomoses, with an occasional reinforcement by a Halsted mattress suture, gave us an immediate operative recovery in every instance. On the day following the operation the animal would usually appear ill, but by the second day stools were passed, and after three or four days the appetite was good and there was a regular daily passage of fæces. In the first week diarrhœa was often present, but this soon subsided and the stools became normal in consistency. For a time the animal would remain normal in weight and general condition, but sooner or later signs of emaciation would appear with progressive loss of weight until the animal was chloroformed. This in one instance was 123 days after the operation.

We believe that the animals could be kept alive indefinitely with proper regulation of diet, for at autopsy the large spindle-form enlargements at the upper anastomoses were distended by impactions of solid materials, such as fragments of bone, hay, etc. (Fig. 19), forming an almost complete obstruction. The experiments of Mall, in which glass balls were placed in the food, but were not as a rule passed in the stools, show that solid, non-digestible masses do not pass through the reversed loop. The more soluble food stuffs, on the other hand, easily pass as is evidenced by the regular movements and by the contents of the bowel at autopsy.

That antiperistalsis can occur is evidenced apparently in clinical cases of intestinal obstruction by the fæcal vomiting, though in an obstruction high in the small intestine regurgitation might readily be caused by a strong general contraction of the gut above the obstruction, and by the pressure resulting from spasms of the abdominal wall. However, if the obstruction is low, antiperistalsis alone will explain the presence of intestinal contents in the stomach.

Cannon and Murphy (8) (1906) in their valuable paper on intestinal movements, have stated that it is "probable that a direct study of peristalsis in animals in which obstruction and stasis of food have been caused may prove that in such conditions reversal of the normal direction of peristalsis readily occurs."

We undertook at varying intervals after the reversal of portions of the bowel to make a direct study of the peristalsis, at the same time bearing in mind the statement of Meltzer and Auer that the mere opening of the peritoneal cavity tends to inhibit gastric and intestinal peristalsis. The animals under ether narcosis were placed in a tub of normal salt solution at a temperature of 37° C. and the loops of bowel allowed to float free. Small quantities of a 1 per cent pilocarpin solution were then injected intravenously.

In one of these observations, twenty-four days after the operation, active peristaltic waves would sweep down to the upper line of anastomoses, and then the mere suggestion of a wave would pass on down over the loop. A fairly distinct wave would occasionally start up the loop, though at no time was the peristalsis as active in the loop as in the normal gut. There was evidently a local disturbance of the peristaltic activity. Similarly, in another case, eighteen days after the operation, with twenty-eight inches of bowel reversed, a peristaltic wave beginning 6 cm. above the upper anastomosis would seemingly stop at the line of suture, and be followed by a feeble movement which would continue from the upper anastomosis down toward the lower. Pinching of the loop started waves which passed downward, but they were more sluggish than those started by a similar stimulus in the normally directed intestine. Thus downward peristalsis in the loop was at all times less definite than in the remainder of the intestine.

In another experiment a wave would pass down to the upper line of anastomosis, where, stopping abruptly, it would jump to the lower line of anastomosis and pass upward along the loop.

In one series of observations the large intestine, in which antiperistalsis normally occurs, was reversed. These animals invariably developed peritonitis, although at autopsy the reversed loop was found in each case to be perfectly healthy and the suture intact. The infection was due to necrosis and sloughing of the portion of the rectum between the lower line of anastomosis and the anus, in which vascular anastomoses evidently were insufficient to maintain life in the short terminal portion of the bowel not reversed. To obviate this we hope to completely excise the lowest portion of the rectum which cannot be reversed, and bring down the lower end of the reversed loop and suture it into the anus.

In concluding, we agree with Kirstein that some antiperistalsis does take place, but we believe that the propulsion of the fluid or semi-fluid contents through the loop is partially caused by the strong contraction of the hypertrophied portion of the gut adjoining the upper suture. The contents are thus forced

well down into the loop, whence their fluid portion is carried onward through the reversed segment by antiperistaltic waves, whereas the more solid portion is carried back up into the dilated part of the gut by the normally directed waves.[1]

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Prutz and Ellinger: Ueber die Folgen der Darmgegenschaltung, Archiv. f. klin. chir., Vol. LXVII, 1902, p. 964.

[1] The paper of Edwin Beer and Carl Eggers (Are the Intestines Able to Propel their Contents in an Antiperistaltic Direction?—Annals of Surgery, Vol. XLVI, p. 576, October, 1907) has appeared since the writing of these notes. From their observations of the behavior of reversed loops, they are convinced "that the small and large bowels are capable of propelling food in an antiperistaltic direction." "Early in the life of the reversed loop, there seem to be ana- and katastaltic waves; later on the katastaltic (which are antiperistaltic with reference to the original normal bowel) seem to predominate."

Their conclusions are in accord with our own and serve to strengthen the view that antiperistalsis does occur, though we believe that the vis à tergo does play more part in forcing the contents through the loop, or at least well down into the loop, than they attribute to it.

XVIII. PRIMARY SARCOMA OF THE HEART IN A DOG.

BY CARL HERBERT BRYANT.

Owing to the great rarity of tumors of the heart, especially of those forms which are not of metastatic origin, the accidental finding of such a growth seems worthy of record. Particularly in dogs do cardiac tumors seem to be uncommon, and in the available literature we have found no recorded cases.

A large bulldog, a vagrant animal apparently in vigorous physical condition, died under ether anæsthesia early in the course of an abdominal operation for a hypothetical lesion. A somewhat vicious animal, he had been kept under close surveillance during his several days residence in the laboratory, and there were no indications from his behavior that he was ailing in any respect. No auscultatory examination of the heart and lungs had been made.

In view of the fact that in a number of instances of sudden death under anæsthesia in the Hunterian Laboratory the cardiac failure had been associated with the presence of Filariæ in the heart and pulmonary vessels, it was anticipated that these parasites might be found in this animal at a post-mortem examination. A careful autopsy, however, resulted in negative findings other than the lesion to be described. A painstaking search for a possible primary focus of malignant disease failed to reveal any abnormality whatsoever in the visceral or in the skeletal structures. Though the usual intestinal parasites common to canines were present there were no Filariæ.

At the base of the heart, lying practically on the inter-auricular septum, at the root of the large vessels, is a roundish, slightly lobulated tumor about the size of a chestnut (Fig. 20). It is largely concealed by the left auricular appendage (lifted up in the photograph) and fits snugly in between the pulmonary artery and aorta without infiltrating their walls. It

FIG. 20.—Photograph of tumor, from which block has been cut for microscopical examination. Left auricle lifted away from its normal position, in which it largely concealed the tumor.

extends around behind the aorta until it touches the base of the superior vena cava. The growth measures 3.5 x 1.8 x 1.3 cm. in its various diameters, the longest diameter being situated antero-posteriorly. The growth is firm, sessile, and its surface is covered by glistening epicardium. Its blood supply is abundant.

On section the surface is smooth, gray, yellowish-red in its more vascular areas, somewhat translucent, and fairly homogeneous in structure. It nowheres infiltrates the subjoining structures and evidently originates in the sub-epicardial connective tissues.

Microscopical appearances.—The tumor proper is surrounded by a fairly thick layer of vascular connective tissue. From this capsular layer interlacing bands of fibrous tissue pass into the growth, partitioning it into lobules of variable size. In a few areas there seems to be some proliferation of the spindle cells of these septal strands, but otherwise the tumor consists of alveoli of round cells, reproducing the small round-celled sarcoma in its pure form. The cells are of medium size with large, deeply staining nuclei. In most places the groups of cells are alveolated by the fibrous septa, but in some fields there are diffuse areas where there is only a delicate intercellular network with a few thin-walled blood-vessels. The cells are nowhere pigmented.

Thus the tumor presents the structure of a typical round-celled sarcoma. The heart was otherwise normal. There are no endo- or myocardial changes and evidently the growth had not reached a sufficient size to cause any functional disturbances from vascular obstruction.

The literature concerning tumors of the heart deals almost wholly with those which have occurred in man, though we have found occasional references to their disclosure at autopsy in the hearts of herbivorous animals. The tumors, in a large proportion of the recorded cases, have been secondary to disease elsewhere. In the Index Catalogue of the Surgeon-General's Office, 1st Series, 1884, Vol. V, under tumors of the Heart, are references to about 90 papers. In Vol. VI, 2d Series, 1901, under the same heading occur references to 52 papers in the intervening seven years. These, for the most part, are records of isolated cases, and with but few exceptions describe metastatic tumors. From this the rarity of primary growths may be inferred, and the following figures serve to show that the relatively more common secondary growths only occur in 3 per cent of hospital cases which have had post-mortem examination.

In a record of 4547 autopsies Arthur Willigk (23) in 1856 found 16 cases of cardiac cancer, 9 involving the heart itself and 7 the pericardium. All were secondary and they represented the proportion of cardiac metastases in 477 cases of carcinoma originating in other parts of the body. At the time of his report he found reports of 5 cases of sarcoma and 4 of epithelial tumors (two being melanotic) of the heart. Similar statistics were given in 1874 by Ely (8), who found among 2161 autopsy records in the Georg Hospital during ten years, 7 cases of cardiac tumor, all being secondary carcinomatous metastases. Dr. MacCallum has kindly given us the following figures from the Pathological Department of The Johns Hopkins Hospital: In 2942 autopsies there have been 10 tumors of the heart, all secondary with the exception of one rhabdomyoma. They are divided into 1 sarcoma, 1 lymphosarcoma, 2 epitheliomas, 1 endothelioma, and 4 carcinomas.

Bodenheimer (4) in 1865 gave figures in regard to the position of the metastases, showing that the muscular walls are most commonly affected and with about equal frequency on the two sides. In a few cases, however, the pericardium alone was involved. He explained the variable symptoms which had accompanied the growths as purely mechanical effects of their presence; namely, the precordial pain, palpitation, sense of oppression, dyspnœa, cough, hemoptysis, cyanosis, œdema of the extremities, effusions into the various serous cavities, giddiness, syncope, attacks of unconsciousness, etc.

Fränkel (10) in 1889 collected reports of 17 cases of primary tumors published between 1876 and the date of his writing. To this list Bertenson (3) in 1893 added 13 more cases, 8 of them antedating Fränkel's paper, having been overlooked or purposely not included by him. Among them was Bodenheimer's (4) case of primary sarcoma reported in 1865.

Of Bertenson's 30 cases of unquestioned primary growths 9 were sarcomata, including 3 described as fibrosarcoma and 1 as a myxosarcoma. The others were divided between fibromata, carcinomata, lipomata and cysts. The situation of the growths was as follows: 7 were in the right auricle; 3 were in the right ventricle; 7 in the left auricle; and 5 in the left ventricle; 2 occurred in the sheath of the auricles; and 2 in the sheath of the ventricles.

Tedeschi (9), also in 1893, estimated that 80 cases of primary tumor had at that time been recorded, but it is probable that he included some which were possibly of metastatic origin.

Petit's (18) exhaustive report (1896) deals interestingly with the historical aspects of the question. According to him the first recorded case of "tumor" was a cyst described in 1767 by Lieutaud. Ely (8) believes, however, that the majority of the earlier reports, many of them indefinitely described, were likely enough thrombi rather than true neoplasms. Petit says the first authentic lipoma was described in 1855 by Albers; the first fibroma by Luschka; the first myxoma by Lonne in 1869; the first parasitic cyst by Dupuytren in 1871, and the first sarcoma by Deffaux in 1872. According to Wolbach (24) the first authentic rhabdomyoma was reported by v. Recklinghausen in 1863, and in his recent paper he adds one more to the 11 previously recorded instances of this rare form of primary and congenital tumor.

Of the primary sarcomata a few of the more important cases have been published by Gross (11), Jacobi (14), Fränkel (10) and Hektoen (12). Hektoen's case possesses a remarkable similarity to our own, although the tumor was large, had spread over a large part of the heart and had increased in size to the point of embarrassing cardiac action. It, however, had apparently originated from the subepicardial

tissues and was practically of the same histological picture as this tumor which, in a much earlier stage of its growth, we have found in a dog.

More recently reports of cardiac sarcomata have been made by Leroux and Meslay (16), Lambert (15), Bernheim (2), and Raw (19). Raw refers also to cases of Zander, Hottenroth and some others. Other cases have been included by Ricketts (20) in the bibliography following his paragraphs on sarcoma of the heart. Among them are cases by Sterling (21), Thacher (22), and others which were probably metastatic in origin.

Of the many cases that have been reported, the pathological conditions were those of the terminal stage of the disease, and consequently the growths had advanced to such a point that it was difficult to determine exactly where they had originated, whether in the pericardium, in the epicardium, at the base of the heart or elsewhere. In our case the accidental finding of a small tumor in the situation described may possibly shed some light on the common source of origin of primary sarcomatous growths.

Summary.—Tumors of the heart are rare, primary tumors especially so. Almost without exception the recorded cases have occurred in man and have led to death in consequence of great vascular stasis. The tumor in the present case—a primary epicardial round-celled sarcoma, an accidental autopsy finding—had led to no functional disturbances. We believe it to be the first recorded case of primary tumor in the heart of a dog.

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XIX. NOTES ON THE RESECTION OF LARGE PORTIONS OF THE SMALL INTESTINE.

By HERBERT M. EVANS and A. G. BRENIZER.

Those who have followed the history of intestinal resection will remember that only a few years ago the successful excision of many inches of the small intestine was a matter of comment and unusual interest.

The early experiments of Senn (1), however, clearly showed that about a third of the intestine could be removed without danger either to life or to nutrition, and eventually, in 1899, Dreesmann (2) was able to collect some 27 successful clinical cases in which over a hundred centimeters of the intestine had been resected, two of them, indeed, exceeding three hundred centimeters—the celebrated cases of Fantino and Ruggi.

Since Dreesmann's publication some eight or ten resections of equal extent have been recorded, so that his list must be increased to at least 35 authentic cases[1] in which over a hundred centimeters of the small bowel have been successfully removed.

Step by step with the increasing success of enterotomies in surgery, valuable experimental work in continuation of Senn's researches have given us truer ideas of the possibilities of successful resection in animals. Thus, as a result of his observations Trzebicky (3) was convinced that animals would tolerate the removal of more than a third, and, as is well known, Monari (4) has declared that the limit may be still further extended to seven-eights of the small intestine; for in an animal with this great fraction removed he found no important interferences with metabolism. Observations made by Flint[2] in 1900 are of even more significance in this respect than Monari's single successful case, for three animals, upon which resections of 70, 82 and 83 per cent respectively had been performed, were alive many months after the operation.

Thanks to the investigations of De Filippi (5), Plaut (6), Riva Rocci (7), Sagini (8), and Erlanger and Hewlett (9), we are now aware that we need fear no serious embarrassment in the digestive or assimilative powers after such resections, if due attention be paid to the amount and kind of food; for practically all are agreed that the only impairment in such cases is in a diminished power of fat absorption. Whether this loss, dependent on a diminished area of absorbing lymphatic radicles, may not ultimately be largely regained through hyperplasia of the mucosal lymphatics remains as yet unknown.

The recovery from such a tremendous loss of secretory and absorptive surface has been made more intelligible to us by the demonstration of a compensatory hypertrophy of the intestinal wall, which follows these operations—a hypertrophy first noticed by Senn, but not thoroughly studied, so far as we are aware, by anyone but Flint, whose results are as yet unpublished.

Our own resections were undertaken with quite another object than that hitherto sought; viz., to study the essential vascular changes in the hypertrophy following resections—an investigation begun by one of us in the laboratory of Professor Mall. Quite apart from such interests, our operations have taught us certain things not only in regard to the possible limits of resection, but also as to the behavior of the animals under investigation, and owing to the few observations in this field these facts are here set down.[3]

Before the very extensive operations were attempted a number of lesser resections were made. Excluding the few cases in which peritonitis supervened these animals invariably survived. In four of these successful cases 33, 37, 41, and 50 per cent respectively of the mesenterial intestine was removed. The animals behaved alike in all essential respects, so that the relation of one case, No. 4 in our series, will suffice to illustrate the subsequent history of all:

Protocol, No. 4. White male dog with black spots, weighing 21 pounds and apparently in the best condition. On November 27, 1906, the abdomen was opened under ether anæsthesia near the outer border of the rectus. At a point 42 cm. from the duodenojejunal flexure a piece of intestine 105 cm. in length was resected. On measurement just 105 cm. of gut were left in the distal piece, so that the entire mesenterial intestine was 252 cm. in length (measurements were made with a piece of cloth, the length of which was used as a unit and afterwards accurately measured). The distal and proximal ends of the gut were then inverted and a lateral anastomosis was made. The abdominal wound was closed in layers. The dog made an uneventful recovery.

For twelve days the animal was fed three times daily on milk and pulverized crackers. The wound healed per primam, and on the fourteenth day the animal was turned out into the general yard. Here, though he undoubtedly got more than his share of the daily meals, he grew progressively thinner. On one occasion we confined him again in his cage, forcing the food in the hope of increasing his weight, but this made little appreciable difference and by the end of the twenty-second post-operative day he had become greatly emaciated. His thin appearance, however, was in strange contrast to his persistently voracious appetite and general spirit and activity.

For the first five days there were traces of blood in the stools; the movements subsequently became soft and mushy in consistency. Occasionally, lasting for a day or two, a troublesome diarrhœa would appear, but this was infrequent.

After the twenty-third day our records showed no further diminution in the animal's weight. There followed a gain in weight, which manifested itself without increase or change in any way

[1] These have been collected mainly from those listed in the Catalogue of the Surgeon-General's Library (New Series) and from the Index Medicus.

[2] Metabolism experiments on these animals were reported by Erlanger and Hewlett. Professor Flint has manifested the greatest interest in our experiments and has most kindly aided us by his suggestions.

[3] Most of our operations were done in conjunction with Dr. L. L. Reford, to whom is due not a small amount of what measure of success was attained.

in the diet, and was a constant feature from that time on. He always appeared to be the healthiest and most active animal in the paddock. His appetite was tremendous and he would often bolt down quantities of food, as though fearful of not getting his share of the provender if more time were taken. He would often keep his companions from the food, and was so vicious in this regard that he became extremely objectionable in the yard.

On April 10, 1907, 134 days after the resection, the animal was chloroformed and autopsied, in order to study the changes which had taken place in the intestinal tract. We found much of the abdominal cavity occupied by an immense loop of bowel, which showed at many points the fine black interrupted sutures of our old anastomosis, demonstrating that the hypertrophy, which was remarkably local, had occurred chiefly in the neighborhood of the anastomosis. On either side of the hypertrophied portion of bowel, which assumed a spindle-shaped form, the enlarged bowel rather abruptly narrowed again to its normal size. Measurements above and below the seat of anastomosis showed little change in length from the records made at the time of operation.

In the accompanying charts the ordinate values represent weight (a pound being the unit), while the abscissæ represent time (a period of two days being the unit). The chart plotted for this animal (Chart 1) gives the typical behavior in these cases. The rather speedy emaciation and then gradual increase in weight are plainly marked and the same thing occurred in the case of each individual of the four. The others, however, were more tardy in again attaining their normal weight. Since we did not autopsy animals at varying periods it is impossible to say that the beginning of the rise in weight marked the beginning or achievement of a certain amount of compensatory regeneration, though this is not improbable.

The more extensive resections with their outcome may be briefly tabulated as follows:

Animal No.	Length of mesenterial intestine.	Length resected.	Percentage of intestine resected.	Ultimate result.
6	250.5	168	76.1%	Recovery.
10	189.0	160	84.6%	Recovery.
11	170.0	147	86.5%	Death in 30 days; definite evidence of "hypertrophy."
13	182.0	159	87.3%	Death in 51 days; little or no evidence of "hypertrophy."
9	263.0	242	92.0%	Death in 97 days; no evidence of "hypertrophy."

The weight curve during recovery from such extensive resections is equally well illustrated by that plotted in the case of Animal No. 4. It is to be observed (Chart 1) that the rather rapid emaciation is not succeeded by a really persistent gain until well after the 28th day. The gain is decidedly gradual and in the case of No. 10 many more weeks were consumed before the normal weight was approached.

Animals Nos. 11 and 13 showed considerable difference in their resistance to the resection, for, though originally of the same weight and receiving the same post-operative treatment, the one emaciated rapidly and the other much more gradually.

Animal No. 9 in the series (Chart 2) from which over 92 per cent of the free intestine had been removed with perfect and immediate recovery, was followed with the greatest interest. The animal, considering its size, was very fat—a factor which no doubt contributed largely to the long resistance to marasmus which showed in a post-operative life of over 97 days. She had always been active and had eaten well from the second day after the operation. The decrease in weight—not so rapid as in other cases—continued in spite of several periods of special feeding which we enforced. Except for two marked, but temporary oscillations, shown in the chart, the fall in weight was constant, though more gradual as the weeks passed.

Conscious that the animal had already shown a post-operative life in excess of any previously reported after so great a resection, we were in hopes of staying the emaciation for a length of time sufficient to afford ample opportunity for intestinal hypertrophy. With appetite, good spirits, activity and every appearance of health save a profound emaciation the animal at length died. Only for the last three or four days did she exhibit any evidence of weakness or signs of physical illness.

At the autopsy no more remarkable instance of atrophy could possibly have been presented. Not only were there no evidences of a hypertrophic response in the gut, but all of the organs and notably the liver and spleen had diminished to a small fraction of their normal weight and size. Microscopic examination showed pictures everywhere of cell shrinkage and destruction with an accompanying accentuation of the connective tissue framework.

It is clear that in this case we had exceeded the limits of successful response. In the other cases it may fairly be said that bountiful overfeeding for many weeks and months might, in all probability, have changed the eventual outcome. If our short experience has taught us anything, it would emphasize the necessity for abundant nourishment and the best hygienic surroundings and care. With these precautions animals will surely survive resections in an amount heretofore not thought possible.

A word may be said concerning the hypertrophy found in certain of the cases just described. We were much impressed by the findings after certain other operations upon the intestine done in this laboratory during the last year. Thus, in the obstruction produced after the reversal of a loop of the small gut we saw a dilatation remarkably like those in our own cases. The excellent figures of a typical one of these reversal cases given by McClure and Derge (Figs. 17-18, Pl. XLVIII) might serve equally well to illustrate our own findings. It is significant that in both cases one finds an hypertrophy of the intestinal wall. These things lead to the consideration of whether we could not explain the great changes in the intestine as a result of a certain amount of obstruction which our anastomosis necessitated. Against such a view, we have found little food in the distended bowel, not, indeed, anything indi-

cating an obstruction. So striking, however, was the similarity of the autopsy conditions in these cases that we must now institute careful controls in which a series of anastomoses without resection can be studied after a considerable post-operative life, and in other cases we must study similarly the effect of slight obstructions.

In conclusion it may be said that, excluding surgical mishaps, animals undoubtedly can invariably survive the loss of a third of the small intestine and practically always the loss of half.

With the best of care many will tolerate a removal of two-thirds, and some, as Monari's, Flint's, and our own observations indicate, will recover from a resection of almost seven-eighths of the mesenterial intestine. This, however, certainly approaches the limit of subsequent compensatory hypertrophic response.

What is meant by recovery may well be defined, for a post-operative life for any period of days or weeks can not be a criterion; nor can an external appearance of activity and health, judging from our own experience. For example, Animal No. 9 in our series was in no sense a "recovery," though it survived the operation for almost a hundred days with no evidence of weakness or ill health until shortly before death.

A return to normal or nearly normal weight may be delayed for many months, and it is only when this is approached that we may justly speak of true recovery. Even though in some of these cases there may remain a tendency to diarrhœa and a need of careful regulation of the diet, these observations furnish us nevertheless with astonishing examples of the compensatory powers which the body possesses in adjusting itself to abnormal conditions.[1]

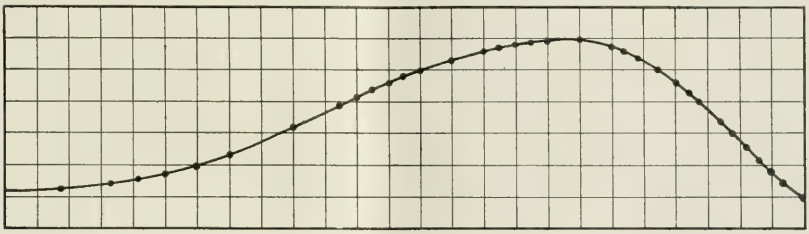

CHART 1.

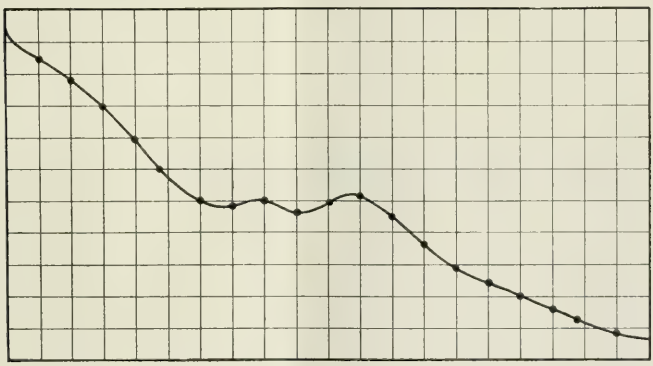

CHART 2.

[1] There was one peculiarity of these animals not mentioned by the writers which struck me most forcibly; namely, the astonishing change in their disposition. Animals previously amiable and friendly, after these resections would often become belligerent and ferocious to a degree. When allowed to run free in the paddock they would without provocation attack any animal they encountered, regardless of his size; and they were oblivious to punishment. One of them killed a number of other and larger dogs, so that he had to be muzzled, and if the chance offered would fearlessly attack them even when thus handicapped. Indeed, we thought that this restless activity played not a little part in keeping the animal thin. It undoubtedly represents some psychic consequence of the disordered nutrition. I am told that somewhat similar characteristics may appear in animals after the establishment of an Eck's fistula, when they are allowed to have a proteid diet. I have never seen a change in disposition result from any other operation, except the direct removal of the frontal lobes.—*H. C.*

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THE PHYSICIAN IN THE PAINTINGS OF JAN STEEN.

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The paintings of Steen date from that period of intellectual activity which we may roughly describe as the seventeenth century; and some contemplation in retrospect of the setting in which they were produced must needs be undertaken if we are to bring to them and to the man who painted them the interest and appreciation which both deserve. Though the story of those days is never quite a stale one it is of course an ancient tale; and this difficult task of leaping the years is one, I dare say, we usually do awkwardly enough. But it so happens that sufficient facts are at hand to enable us to construct a fairly satisfactory picture of the age in question. We are well aware what, in a general way, those facts are, and the term Renaissance, under which we group them together, is a hackneyed one; yet I imagine we seldom clearly appreciate and can indeed hardly exaggerate the buoyancy, the elation, the zest, the new interest in life which characterized those days and led, in the end, to all those results now spoken of in a more or less off-hand way. We are wont to proclaim the strides which Progress, shod in her seven-league boots, has made in our own days; and to point with pride, for instance, to the infinite distance she has travelled from Jane Austen to Henry James; but consider for a moment a few of the achievements of the seventeenth century which indicate the extent of general interest in natural science and the scientific method, as well as the importance of medicine. These were the days, for instance, of the births of academies: the College of Invisible Philosophers dating from 1645 and to be christened the Royal Society when it came to term, the "Académie des Sciences," the Experimental Society, and others in Italy. These were the days of philosophers of the first rank: Bacon, Locke, Descartes, Spinoza. They were the days, too, of new scientific appliances, like the microscope of the Jansens of Holland. And as for scientific discoveries, the times teemed with them—ranging all the way from the discovery of the circulation of the blood to that of the site of cataract. You have indeed but to name over some of the medical men of this time to remind yourself how lively must have been the medical interest and enthusiasm. Borelli, Malpighi, Bellini, Harvey, Glisson, Wharton, Willis, Cowper, Vieussens, Brunner, Bartholinus, Pacchioni, Sydenham, van Helmont, Mauriceau, Chamberlen—even so incomplete a catalogue as this suffices for the purpose. You must, indeed, think of the men of these renascent days as fired with enthusiasms which make those of even our own somewhat spirited times look jaded. You may imagine them facing the new world which had just been handed over to them for their very own with all the rejoicings of strong men about to run a race, or the chafing eagerness of war-horses scenting the battle; but perhaps thinking of them as children before the nursery door on Christmas morning gives you as good a picture of the facts as any figure can. The nursery, every one knew, was full of treasures—could they not indeed hear the tables creaking and groaning under the good things? And could they not imagine the feast spread in the rooms beyond, the feast that would end with Harvey's "divine banquet of the brain?" No wonder, knowing as they did where the door was and how to open it, after the long night from which they had just awakened, they fretted to be within. No wonder, too, that once in the store-house of treasures a hubbub arose—inordinately boisterous laughter, whinings, bickerings—each child forgetting his manners, forgetting his neighbors, forgetting, in his excitement, everything but the enthusiasm of new delights, the joy of new possessions. You could scarce hear yourself think for the squabbling of the Iatrophysicists and the Chemiatrists; van Helmont ran to and fro shouting for everyone to look at his "Archeus"—a man-like toy that walked and talked without winding; and Descartes and other Gallic children, with all the zest and with some of the petulance of little boys, tried to get Harvey to throw away as worthless one of the treasures on which he had written his own name.

It was over the Netherlands, among other places, that the new spirit chose to brood and here it was that some of the greatest results were achieved. The little countries were, as it happened, sharing with Italy, France and England an immunity from a struggle then raging on the Continent; and freed from the demand of war they yielded to the soft call of

FIG. 1.—Love-sick Lady, or The Doctor's Visit (Smith, No. 118); now in the Mauritshuis, The Hague; restored thither from the Louvre in 1815; until 1763 belonged to the Collection Lormier; until 1771 belonged to the Collection Braamcamp.

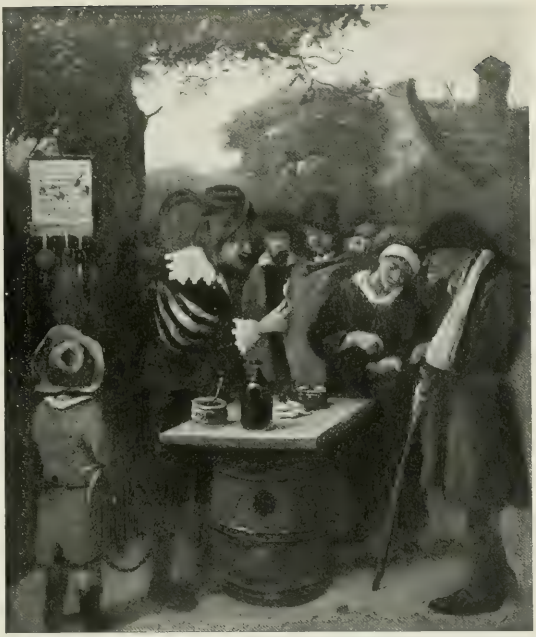

FIG. 3.—Der Wunderdoktor—The Rijks Museum, Amsterdam.

FIG. 2.—The Quack Doctor (Smith, 47); now in the Rijks Museum, Amsterdam; until 1763 belonged to the Collection Lormier.

the arts of peace. Here the incisive author of La Méthode had chosen to live; here Spain's God-intoxicated philosopher was raising his voice to a world that later was to pause, to listen, to ponder, and to bow the knee; here Huyghens was teaching the clocks of the world to tick out the name of Holland to eternity. And if we turn to medicine we find the little folk as industrious as ants. Here was Boerhaave becoming, as Haller called him, the teacher of Europe (communis Europæ præceptor); here was Beverovicus of Dordrecht, the first physician to come out for Harvey; here were Sylvius, of cerebral fame, and the Jansens, inventors of the microscope, and de Graaf, discoverer of the follicles, and Nuck the anatomist, and Ruysch, and Swammerdam, and Leeuwenhoek.

It was, as it happened, in the industrious little Netherlands during those enthusiastic times, that one of the great schools of painting sprang up; and it is interesting to trace with Monsieur Taine, who applies to painting the same method that he used for literature, with equal brilliance, though with no less exaggeration, the characteristics of this school from the nature of the people among whom it came into being. They were, we are reminded, essentially a Germanic race, lacking in their features sculptural nobleness and dignity and in their minds finesse and precocity. They were voracious, carnivorous, addicted to drunkenness, sluggish and torpid in impression and movement; "stiff", says a Toulousian in criticism of them to M. Taine, "stiff, frigid, with no sensibility or sentiment, dull and insipid, perfect turnips, sir, perfect turnips." In Italy, in France, on the other hand, people were precocious, witty, but only moderately capable of biding their time, of self-subordination, of maintaining order. It is an Italian noble lady, for instance, who exclaims on eating a delicious ice-cream, "What a pity there is no sin in it!"; and it is a French lord who says of a roué, "Who wouldn't admire him, he's so wicked?" The defects of Germanic wit have, however, their strong points. The Germanic peoples are housekeepers who love their households; they are the great laborers of the world; they are able to accommodate their tranquil mind to comprehending things and directing them. The great natural difficulties of their lands they are able to overcome, turning Belgium, an alluvial expanse, and Holland, a deposit of mud surrounded by water, from being dwelling-places for storks and beavers into habitations for man. And these struggles, together with those against the unpropitious soil and rigorous climate end in making them excel in the useful arts, but in being deficient in profound philosophy or elevated poetry. All this produces good sense, somewhat limited; happiness, somewhat gross. "A Frenchman would soon yawn over it, but he would make a mistake; for this civilization, which seems to him unctuous and vulgar, possesses one sterling merit—it is healthy; the men living here have a gift we [the French] lack the most—wisdom, and a compensation we are equally undeserving of—contentment."

You do not need to accept all that M. Taine says or to follow him in such absurd details as the effort to make the rigorous climate of the Netherlands responsible for the absence of the nude in Dutch art, to realize that the contrast he draws between the German and the Latin races is well drawn and that in a general way the characteristics he speaks of did come out in the painting of the Dutch.

We are prepared by this time to expect that a school of painting flourishing in the seventeenth century should show some definite reflection of the scientific and medical interests which were taking such a prominent part in the thought of these days and of these peoples; and this is in fact the very point I wish to make. You will think at once, of course, of the famous, the almost hackneyed, Rembrandt, "Die Anatomie," but I refer you, by way of preface, to the less-known dissection of the head by the same painter; to the splendid "Anatomische Vorlesung," by de Keyser; to the "Anatomies," of Bäcker, of Van Neck, and of Pietersen; to the "Surgeon's Guild," of Quinckhard; and to other similar pictures, fifteen of them, now in the University of Amsterdam. I do not think, however, that these pictures so much represent the interest of the painters in medicine as they do speak for their large duties as portraitists; and it is to the school of little Dutchmen we must turn—little only by comparison with their great contemporaries—to see Dutch medical painting as a reflection of Dutch life and interests.

These "little Dutchmen" were a most interesting group of men. They were perhaps among the first to paint an entire picture from nature. They practically had no studios and they got along without models. They were, many of them, tavern habitués to whom nature appeared excellent. They were satisfied with mere living. They did not paint subjects as curious or interesting specimens, nor charge landscapes with the subtleties, refinements and emotions of poets. They were, I should venture to say, realists—though without any conscious theory of the thing. They moved among the people, painting what interested them just as they saw it. And it happened that what interested some of them greatly—Dou, Ostade, Teniers and Steen in particular—was the medical life they saw about them. It is of the last of these four that I wish to speak in detail.

The facts of Jan Steen's life are paltry enough. 1626, the year of Bacon's death, brought him into the world, nine years ahead of Rembrandt. He began the study of painting under Knüpfer at Utrecht; pursued it under Ostade in Haarlem, and finally at the Hague under van Goyen—marrying the latter's daughter in 1649. He had some not very distinguished residence at the University of Leyden, where culture made of him, as Holländer puts it, a "genius of brawling, drinking and painting." In 1672, having meanwhile had a somewhat precarious career on the financial side, he opened a tavern at Langeburg, near Leyden; one year later he married for the second time; and in 1679 he died. His pictures were evidently not highly esteemed during his life; they brought low prices, were probably given by him in exchange for liquor, and were to be found in almost every liquor shop and cabaret in Delft. There was hardly anything in this commonplace existence—and that it was a vulgar existence, too, there is strong tradition, though the portraits of him belie the story that he was a common drunkard—to account for a notable artistic

career; yet such a career he had. He was a painter, beyond doubt, of very great power and he had fortunately in his youth refined friends—among them Mieris and Metsu. Steen was not a satirist, in the sense that Hogarth was a satirist, for he made vice attractive by beautiful workmanship. He was capable of the very best; but he frequently painted in a slip-shod manner (probably after drinking); and his later work is often vile in subject, generally vulgar and loose, and slovenly in execution.

I can find no specific cause for the way in which medical subjects appealed to him. He painted, in all, about 315 pictures, and about 32 treated of the physician in one or another of his activities. Even Teniers, who was also partial to these themes, came nowhere near this proportion—painting, out of a total of 685, only about 30 medical pictures.

It is of course of particular interest to see just what features of the medical life appealed to this genre painter. We are not surprised to find him attempting nothing so ambitious as some of the great anatomies. His taste was as a rule not so elevated; he found no pleasure in conventional groups; and the small humorous canvasses which he left behind (they are usually not over 2 ft. square) were the work of a humorist, a genre painter who might excel only on condition that he take his limitations into account. It is fortunate that his taste did lead him to take them into account, and that he did not burn his artistic wings by soaring too near the sun—a fate that Hogarth, the "English Steen," did not wholly escape.

I am rather surprised first of all to find no blood-letting scenes among the Steen paintings I have seen, nor so far as I am aware among his pictures at all. The practice was surely rampant nor was the subject entirely neglected in art (for instance, two pictures by Brekelenkam and Van der Neer); yet Steen, with all his zest, seems never to have cared to "catch" it. He showed, on the other hand, an overweening, an inordinate interest in a certain form of neurasthenia; and ten "Love-sick Ladies" appear among his paintings. I think likely, too, from the accessories in some of his other works entitled "Sick Lady" or "The Doctor," etc., that he meant to indicate the grand passion as an etiological factor here too. (See the Cupid in pictures 10 and 11.) He usually indicated his meaning by some detail of these paintings (as in the "Rape of the Sabine Women" on the wall of his "The Love-sick Lady"—picture 1); and he either painted them with the refinement and finish of his early life (pictures 1, 9, 10, and 11), or in the more vulgar mood characteristic of his later days (picture 7). Sick ladies in general seem to have found a weak spot in Steen's heart. One grows quite used to the pathetic seated figures, dressed in ermine-bordered sacks —often brilliantly colored and models of taste beside the hideous things that go by that name to-day; to the silk skirts, again often brilliant; to the lovely heads, the sickest of eyes, and an appealing look that none but a boor could resist; to the stately physician taking the pulse as though he were dancing a minuet; to the rich Turkey rug, and the Cupid, and the dog, and the patient's fond mother, and the other accessories.

When we come to ask how these Dutch painters were impressed by disease and its treatment we are not surprised to find a strong emphasis laid on the physician as urologist. One gathers indeed from these pictures that the urine and the diseases of its organs were the chief practical concerns of the medicine of the day, and that diagnosis consisted in courtly palpation of the pulse and a wise look at a urinal. We have, of course, evidence from literature that the facts were not far otherwise. You will remember how the host in the "Merry Wives of Windsor," addressing Dr. Caius, cries out, "Thou art a Castilian, King Urinal!", and a little later in the same scene addresses him as "Monsieur Mock-water."[1] You will also recall in what terms the page of Falstaff brings him his bill of health from his physician. "Sirrah," says that man of war, "you giant, what says the doctor to my water?" And the page answers, "He said, sir, the water was a good healthy water; but for the party that owned it, he might have more diseases than he knew for"[2]—a diagnosis, in view of this patient's checkered and promiscuous career, that was probably quite possible even after no more thorough an examination than simply casting the wise eye on the urinal. Urinary examination had, too, in these days, an importance not now recognized; an importance, as a test of past life, reflected in a painting of this time by the appearance—much to the disgust of the female concerned and of her irate father—of a human embryo in the urinal; and by the Latin saying of the day: "Vulva dolet, urina docet."

Steen and his colleagues did not overlook the quack. You find Steen representing him, in some of his most characteristic but not his most finished paintings, as a rather low order of being, exhibiting his wares or his skill in the open air. He often has a heavily-sealed diploma in prominent display—preferably written in Hebrew; and the crowd which has gathered to hear and to see him gives the artist a splendid chance to exhibit his skill in painting the bizarre Dutch types which appear in these pictures in such profusion (pictures 2 and 3). The same subject attracted Gerard Dou, who, without missing any of Steen's detail, attained a finish that the latter apparently deemed the theme unworthy of. To see, however, how the quack may be treated adequately and yet with exquisite elegance, one must turn to Hogarth's well-known picture in the "Marriage" series of the London National Gallery.

There is a splendid portrait of a quack by Franz Hals, the younger, in the museum at Rotterdam, in which the operator is pictured as removing a small tumor from a patient's forehead; and this removal of glands, or sebaceous cysts, from various portions of the head and neck is a subject not overlooked by Steen. (Picture 4 represents the treatment, and picture 5 the dressing, of such a case.) These pictures reflect a popular belief of the time; for there was a common saying in Holland in the sixteenth and seventeenth centuries which

[1] Merry Wives of Windsor, Act II, Scene III.
[2] Henry IV, Part 2, Act I, Scene II.

FIG. 4.—The Operator (not listed in Smith)—Boijmans Museum, Rotterdam.

FIG. 5.—The Operator (listed in Smith's Supplement, No. 16, as The Village Doctor)—Royal Museum at Brussels. Subject: Removal of a plaster from patient's neck.

FIG. 6.—The Dentist—Hague Gallery. (A similar picture is listed in Smith's Catalogue Raisonné as belonging to the Collection Lormier.)

FIG. 7.—Love-sick Lady (Smith, 119)—Collection Steengracht, The Hague.

FIG. 8.—The Visit of the Physician (known also as Liebestoll)—The Imperial Ermitage, St. Petersburg.

FIG. 9.—The Sick Lady (Smith Supplement, No. 8)—Now in Rijks Museum at Amsterdam, originally in the Collection Vanderhoop. Woman in silver-grey silk jacket with ermine border; skirt of yellow silk.

FIG. 10.—Sick Lady (Smith, No. 146)—Alte Pinakothek, Munich. Woman in scarlet velvet jacket with ermine border; skirt of bluish-gray silk.

FIG. 11.—Doctor Feeling Lady's Pulse (Smith, No. 114)—Now in the Mauritshuis, The Hague; restored thither from the Louvre in 1815. Woman in blue jacket with ermine border; skirt of green silk.

ran: "He has a stone in his head," and the meaning of which was, "The patient is crack-brained." "Cutting the stones from one's head" was therefore supposed to be curative for mental deficiency. The saying, which originated from the romance of King Arthur, was of common occurrence in the farces of the time; and it is little wonder that this reflection of it is to be found in the canvases of Steen.

The dentist, too, was not without his interest for this school. He is the subject of one of Steen's rather good groups (picture 6); of a curious outdoor scene by Victors; of a typical but uncanny interior by van Ostade, and of one of Dou's wonderful candle-light scenes; but these pictures throw no particular light on the medicine of the time.

What light, on the other hand, do the pictures of Steen and his school throw on the *physician* of those days—on the physician as a man, on his standing in the social, his place in the intellectual, life of the times? He is surely, I think we may answer first of all, no longer a barber. He has become a gentleman and his profession is now, whether respected or not, at least respectable. He may indeed be, as we have seen, a wise-looking crier in the markets, with his Hebrew diplomas and all the vulgarity of a peddler; or he may even be a coarse reprobate leading his vulgar life within the pale of legitimate practice (pictures 7 and 8). But he is neither always nor characteristically these. He is on the contrary a courtly, mild-mannered, well-dressed gentleman. He moves about the sick-room with grace. He has none too many scientific resources; but though he has little to depend upon beyond the finger on the pulse and a glance at the urine, he has made himself a place, among his patients, of honor, of dependence, and of affection. Medicine is, in a word, finding in him for its service a good type of man.

Steen, it is true, with all his interest in the medical profession, did not gloss over defects he saw in its professors; yet I think Holländer, who insists that "Steen sought to make the physician laughable wherever he could," rather overdoes the matter. Such a picture for instance as the Amsterdam "Die Kranke Frau" is surely not open to any such criticism. We know, indeed, how bitter satire against the physician could at this time be; vulgar, far from subtle and often tasteless pictures were drawn ridiculing him in every phase of his work; and it is to my mind striking that Steen, with his keen eye, and his shameless humor, did not make the physician more ridiculous. Unlike the satire of Molière, which was directed chiefly at the physician, that of Steen was very much concerned with the patient; if it struck the doctor at all it was only with an incidental, glancing stroke. In his frequent pictures of love-sick ladies his bitter laugh is for the ladies themselves; for the physician there is either no laugh at all or else a good-natured smile. It is indeed, for a painter of such coarse possibilities, a rather fine type of man which Steen in his best moods has recorded as practicing medicine in these times.

If we go to Gerard Dou we find the same testimony. Titian, with his magnificent Parma physician, and Holbein, with his equally splendid Chamber's portrait, had indeed already shown us what type of man medicine *could* appeal to. The message of the Dutch painters on this point is that as a matter of fact, and on the average, medicine in the seventeenth century *did* appeal to men whose intellects, manners, and bearing are worth study.

A list of the medical pictures by Jan Steen, with their numbers, according to Smith's "Catalogue Raisonné" follows:

1.	The Dentist	No. 8
2.	" Water Doctor	" 37
3.	" Quack	" 46
4.	" "	" 47
5.	" Village Surgeon	" 68
6.	" Sick Lady	" 75
7.	" " "	" 77
8.	" " "	" 114
9.	Love-sick Lady	" 118
10.	" "	" 119
11.	" "	" 120
12.	Sick Lady	" 144
13.	" "	" 146
14.	Doctor dressing Leg	" 170
15.	Love-sick Lady	Supplement to Smith " 4
16.	" "	" " " " 6
17.	" "	" " " " 7
18.	Sick Lady	" " " " 8
19.	Love-sick Lady	" " " " 9
20.	Doctor attending Lady, *enceinte*	" " " " 10
21.	Love-sick Lady	" " " " 11
22.	Sick Lady	" " " " 12
23.	Love-sick Lady	" " " " 13
24.	" "	" " " " 14
25.	Village Doctor	" " " " 16
26.	Village Surgeon	" " " " 41
27.	Doctor feeling Pulse	" " " " 88
28.	Mountebank	" " " " 101

Pictures by Steen not certainly identified in Smith's "Catalogue":

29.	Der Wunderdoktor	Rijks Museum, Amsterdam.
30.	Der Operateur	Boijmans Museum, Rotterdam.

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CAMP LIFE: ITS SPHERE OF USEFULNESS AND ITS BENEFICIAL EFFECTS ON GROWING BOYS.

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Throughout the entire United States, summer camps are being formed and thousands of boys spend their vacations in the woods. That this sort of life is beneficial has never been doubted, yet I can find in the literature no scientific reports as to the benefits of this camp life. Also, there are but few popular articles which detail the proper supervision and hygienic surroundings of such camps, and if, as the writer hopes, these camps are to continue to increase in number, there should be more attention paid to their management by the medical profession. As is readily appreciated, the fullest benefits of such out-door life can be secured only if the best hygienic conditions and thoughtful care surround the campers. If several leading camps would report scientific studies of the physical condition and improvement of the boys while under observation, and would outline the daily routine which was found to be most practical in managing the camps, it would undoubtedly greatly aid other camp directors. It is only through such co-operation that hospitals and sanitaria have gained their present degree of efficiency and perfection, and, indeed, to this same cause may be traced the rapid progress in all sciences. So also in camps there should be this "survival of the fittest." Yet the only means at the present time whereby a camp director may ascertain what has been found to be best is by personal inspection, which is in many ways difficult and at times impossible. There should be no more jealousy or secrecy in the methods used in managing boys while camping, than in the treatment of cases in hospitals. During the summer of 1907, I accepted the position of physician-in-charge of "Camp Champlain," Mallets Bay, Vermont, and during the months of July and August closely studied the boys under my care. The results of these examinations are herewith published in order to show the marked benefits of this out-door life, and a rather detailed account of the camp and its management is given in the hope that it may be of value to those interested in the supervision of camps.

Location.—The camp, which has been in existence for thirteen years, is located on a high rocky point covered with pines and surrounded by the waters of Mallets Bay. From one side of this point the water of the bay was pumped through a two-inch iron pipe to the mess hall. The opening of this pipe was about fifteen feet below the level of the bay and perhaps ten feet above the solid rock bottom. There was, I believe, no opportunity for pollution of this supply as all kitchen drainage was emptied into a sand filter on the opposite side of the point. All residue from this filter, and the accumulations of the toilet rooms, which were located at quite a distance from the camp proper, were removed twice weekly to a farm more than half a mile distant. Carbolic acid and chloride of lime were used in large quantities to insure proper disinfection. That the water supply for drinking and for cooking purposes is in no way affected, I am assured, for the two bacteriological examinations of the supply were most convincing.

Camp management.—The campers, about fifty in number, were quartered in twenty-two army tents placed on raised platforms, and as will be seen in the following routine, these tents were inspected each day in order to insure cleanliness and to teach self-reliance. A strict military discipline was maintained, each member of the camp staff, ten in all, acting consecutively as "officer-of-the-day." This officer had entire charge of the camp during his régime, and to him was delegated the duties of inspection and general supervision. The order of the day was:

7.00 a. m.	Reveille. All boys were compelled to arise promptly, take a morning "dip," air blankets and sheets, and dress.
7.15 a. m.	Bugle again blown and officer sees that orders have been obeyed.
7.25 a. m.	Bugler sounds first call for breakfast. Boys assemble on the veranda of the large wooden mess hall, and await second summons.
7.30 a. m.	Call for breakfast sounded. Boys go to their places and await signal by the officer-of-the-day to be seated. Any absence or lateness is noted and investigated. No boy may leave the mess hall before thirty minutes have expired. This regulation also holds for dinner and supper.
8.30 a. m.	Bugle blown for those doing summer study. Perhaps one-third of the campers prepare for college examinations, or are tutored to absolve conditions. All other boys are allowed to boat, fish, or take part in games. During the mornings the two physical directors coach the junior, intermediate, and senior baseball teams. Track work, tennis, and walking are also encouraged.
11.30 a. m.	Fifteen minutes' swim. Supervised by the physical directors, officer-of-the-day and camp physician. All of the younger boys are given swimming lessons, and medals are given later in the season to those showing the greatest improvement at the time of the athletic meet. Any boy who, in the judgment of the physician, is physically disqualified from such energetic exercise or who becomes quickly chilled by the water is allowed only the morning "dip," which consists merely in a quick dive and rapid rub. Several boys who were below the average weight for their age were allowed only the afternoon swim.
12.15 p. m.	Bugle is blown for inspection of tents. Beds must be in order, clothing arranged properly, floors swept, and no paper must be under or around the tents.
12.25 p. m.	First call for dinner. The same general order maintains at dinner and supper.
12.30 p. m.	Second call for dinner.

3.30 p. m. Second fifteen-minute swim. Precautions as at first swim are observed.
6.25 p. m. Bugler sounds first call for supper.
6.30 p. m. Second call is sounded.
7.30 p. m. Bugle recalls to shore all juniors on the lake.
9.00 p. m. Taps for juniors.
10.00 p. m. Taps for seniors. Officer-of-the-day inspects each tent and assures himself that each boy is in bed and that all lights are out. He must also count the boats and at eleven o'clock must again ascertain that no camper is out of his tent.

At first glance it might appear that a day so regulated might be irksome to the boys and that these regulations would be difficult to enforce. That the boys do enjoy this military discipline has been definitely proved by the success of the camp, and by the general feeling of good-fellowship and cheerfulness. Such regularity is in itself an excellent training, and the campers are much benefited by the regular hours for sleeping.

Should occasion arise to discipline a boy there are various punishments which prove most salutary. For instance, when the camp first opens there is apt to be lateness at meals, or perhaps the tents are disorderly, or a boy may attempt to swim at other than "lawful hours." Such an offender is forbidden to boat or to swim for a stated time. Usually two days on dry land is very effective.

Also the query may arise as to how in a camp of so many boys there is not a great infraction of the swimming regulations. That these rules have not been broken is due to two factors. First, the smaller boys are not allowed in boats outside of a chain of islands, all of which are in hailing distance of "Slab Sides," a house built over the water's edge, at which all swimming takes place. Hence these boys do not have any opportunity to take extra swims because one of the camp staff is constantly on duty at this "watch tower," and while primarily he is there to see that the younger boys are always safe, yet at all times he could also make sure that there was no infraction of the swimming rules. The larger boys have a two-mile range of the lake, but word is quickly brought by the campers around the shore of any infraction of rules. Second, the fact that the boys are taught special dives and new strokes in swimming, as well as their love for sport, makes them desire to swim with the rest of the boys. So if a camper be forbidden to swim, he must have rare good luck to get a plunge unnoticed, and he must do so alone, because the spring-boards and good-fellowship of "Slab Sides" tend to keep the campers together.

Beneficial effects of camp life.—As soon as possible after the boys entered camp, a thorough physical examination of each was made and aside from the statistics given later, some interesting facts were noted. About one-half of the campers could not intelligently answer as to the regularity of their bowels. They had no definite time each day for movements, kept but little record as to the frequency or number of these movements, and seemed to consider the whole matter as of little importance. Close questioning revealed many cases where two or three days intervened between passages. Fourteen depended upon cathartics almost entirely, allowing two days or more to pass before considering a movement essential. The headaches, stomach disorders and general malaise to which these boys were subject were in no manner traceable, in their opinions, to any lack of regularty. The dangers and many unpleasant, as well as serious, complications arising from such heedlessness were emphasized, and in the more stubborn cases a careful record was made. It is needless to state that in a few weeks these boys were having regular movements, and that the patent cathartics were no longer necessary.

Yet these boys were of excellent parentage, had physicians of good standing and hence should have learned regular habits at a much earlier time. It certainly seems most culpable in parents to allow their chldren to grow up in ignorance of such important matters, and no matter how proficient or painstaking the family physician may be, he can not always be in attendance nor can he make sure that his instructions are carried out. One instance may serve to recall vast numbers of similar cases. A boy feels unwell, the doctor investigates and decides that the trouble is due to constipation. A purge is given, and the patient is warned about being careful and regular. After, say, five weeks, there is a recurrence of the symptoms and the cause is similar. Now the camp physician holds a unique position. He gives advice and can, by close daily questioning and by constant repetition, finally enforce regularity.

The "method of dining" also occasioned surprise. During the first three days after camp opened, the boys hurriedly bolted their food and rushed back to their boats or games. It really seemed mostly a matter of speed. They had to eat because they were hungry, and they spent as little time as possible in the mess hall. It was then that the thirty-minute rule was enforced. At first there was grumbling because after ten or fifteen minutes the boys were compelled to sit before empty plates and await dismissal. After a short time, however, the boys became more philosophic and ate slowly.

Smoking was prohibited in all cases except amongst boys who had written permission from their parents. What smoking there was, had to be confined to the tents, hence the hero worship which is so frequently found among boys of varying ages tempted none of the younger ones to begin the habit.

Tea and coffee were never given, and at first this appeared to be a hardship. It seems strange that boys ranging from eleven to seventeen years of age should be so fond of these stimulants, and passing strange that they should be allowed several cups of each daily while in their own homes. Whether they will return to these habits after the two-months' abstinence is hard to say. Be that as it may it is certainly a good thing to have them discontinue the use of tea and coffee for even so short a time.

Most of these campers had been living the artificial, unhealthy life of the city, with late evenings spent at theatres or in study, and with comparatively little out-door exercise. Consequently a certain percentage showed at the time of examination a decided anaemia. In order to ascertain the rapid recuperative effects of fresh air, regular hours and

STATISTICAL RECORD OF THE PHYSICAL EXAMINATION OF THE CAMPERS.

Case.	Noted Below.	Date of Examinations.	Age.	Weight in Lbs.	Height in Cms.	Chest Expanded.	Chest Contracted.	Heart.	Lungs.	Specific Gravity.	Color.	Reaction.	Albumen.	Sugar.	Haemoglobin; Sahli.	Number of Red Cells per cmm.	Number of White Cells per cmm.
										Urine.					Blood.		
1	......	July 3	11	72	146¼	70	63½	N	N	1017	c. p. y.	ac	Trace	0	81	4,180,000	4 960
		Aug. 24		77	147	71	62½	N	N	1015	c. p. y.	ac	0	0	94	4,684,000	4.170
2	......	July 3	11	63¾	145¾	67½	62	N	N	1019	c. y.	ac	0	0	92	4,900,000	6,710
		Aug. 24		67	146	70½	60½	N	N	1018	c. p. y.	ac	0	0	98	5,200,000	7,180
3	X	July 3	11	64	136	65½	59	N	N	1022	c. o.	ac	Trace	0	84	4,160,000	8,440
		Aug. 24		66½	137¼	66	57	N	N	1014	c. p. y.	ac	0	0	97	4,896,000	7,670
4	X	July 7	11	55½	131¼	65	59½	N	N	1018	c. p. y.	ac	0	0	62	4,240,000	6,400
		Aug. 26		54½	131½	64½	57½	N	N	1014	c. y.	ac	0	0	91	4,694,000	5,800
5	......	July 5	12	63½	139½	65½	61½	N	N	1016	c. y.	ac	0	0	98	5,100,000	3,880
		Aug. 25		67	139½	69	62	N	N	1013	c. p. y.	ac	0	0	94	4,880,000	8,860
6	X	July 9	12	67¼	132	72	67	N	X	1024	c. o.	ac	Trace	0	103	5,040,000	7,800
		Aug. 26		68½	136½	73	65½	N	......	1013	c. y.	ac	0	0	92	4,485,000	6,940
7	X	July 2	12	67¾	135	69	62¼	N	N	1026	c. o.	ac	Trace	0	85	4,850,000	7,560
		Aug. 25		68½	135½	68½	61½	N	N	1019	c. y.	ac	0	0	91	4,944,000	6,280
8	......	July 7	12	53¾	130	67½	60½	N	N	1020	c. p. y.	ac	0	0	82	4,276,000	8,120
		Aug. 23		58	132	68½	61½	N	N	1014	c. p. y.	ac	0	0	88	4,678,000	7,270
9	X	July 5	12	91	156½	77	69½	N	N	1016	c. p. y.	ac	0	0	93	5,020,000	9,230
		Aug. 24		92½	156½	78	68	N	N	1012	c. y.	ac	0	0	96	5,060,000	8,980
10	X	July 8	12	68½	143	69½	62½	N	N	1014	c. p. y.	ac	0	0	76	4,184,000	8,170
		Aug. 25		73¾	143½	71½	64	N	N	1016	c. p. y.	ac	0	0	87	4,712,000	8,210
11	X	July 7	12	65	148	69	61½	N	N	1017	c. p. y.	ac	Trace	0	81	4,220,000	7,760
		Aug. 24		69½	149¼	69½	60	N	N	1015	c. y.	ac	0	0	92	4,680,000	7,250
12	X	July 3	13	84	149	74	69½	X	N	1012	c. p. y.	ac	0	0	76	3,988,000	8,120
		Aug. 21		87½	149½	75½	68	X	N	1017	c. p. y.	ac	0	0	88	4,984,000	6,780
13	X	July 8	13	64	142½	68	61½	N	N	1021	c. p. y.	ac	0	0	71	4,122,000	7,890
		Aug. 23		68¾	143	69½	60½	N	N	1015	c. p. y.	ac	0	0	88	4,896,000	7,080
14	......	July 8	13	67½	143¼	72½	66	N	N	1018	c. p. y.	ac	0	0	90	4,298,000	6,500
		Aug. 23		78	144	75½	67	N	N	1014	c. y.	ac	0	0	93	4,800,000	7.890
15	X	July 9	13	67	154½	69½	63½	N	N	1019	c. p. y.	ac	0	0	82	4,253,000	8,120
		Aug. 23		74	155	71	62½	N	N	1017	c. p. y.	ac	0	0	86	4,968,000	7,840
16	X	July 1	13	108	169	80¼	74½	N	N	1012	c. p. y.	ac	Trace	0	98	4,960,000	8,430
		Aug. 18		111½	169½	82	74	N	N	1016	cl.	ac	0	0	101	5,020,000	7,980
17	X	July 1	13	92¾	155	78½	74½	N	N	1021	c. p. y.	ac	0	0	84	4,464,000	5,840
		Aug. 18		97½	155¾	80½	73	N	N	1018	c. y.	ac	0	0	98	5,126,000	6,000
18	......	July 2	13	104	162	74	69	N	N	1015	c. y.	ac	0	0	65	4,002,000	8,880
		Aug. 25		115	163½	77	68	N	N	1017	c. y.	ac	0	0	92	4,898,000	8,120
19	......	July 2	14	107	160¼	81½	76½	N	N	1022	c. o.	ac	0	0	104	5,132,000	6,760
		Aug. 26		115¼	165	86¼	75½	N	N	1020	c. o.	ac	0	0	101	5,060,000	7,580
20	......	July 1	14	97¼	154½	77½	72½	N	N	1018	c. y.	ac	0	0	98	5,100,000	8,220
		Aug. 22		102½	155¾	80½	71	N	N	1015	c. p. y.	ac	0	0	103	5,132,000	7,840
21	X	July 2	14	97½	151	80½	72	N	N	1021	cl. o.	ac	Trace	0	81	4,890,000	7,210
		Aug. 23		110	151¾	85	76	N	N	1012	c. o.	ac	0	0	93	4,927,000	9,210
22	......	July 4	14	90½	157½	78½	71	N	N	1017	c. y.	ac	0	0	96	5,420,000	5,980
		Aug. 22		93¾	158½	80¾	69½	N	N	1015	c. p. y.	ac	0	0	92	5,120,000	6,490
23	X	July 8	14	104½	151½	78¾	73	N	N	1020	c. p. y.	ac	0	0	102	5,110,000	4,850
		Aug. 26		100	153¼	82	70½	N	N	1019	cl. y.	ac	0	0	105	5,046,000	7,180
24	......	July 6	14	102	142	74	69½	N	N	1015	c. p. y.	ac	0	0	67	4,460,000	11,400
		Aug. 26		113	142½	78	68¼	N	N	1017	c. p. y.	ac	0	0	94	4,998,000	5,860
25	......	July 9	15	129	175¾	86	77	N	N	1016	c. p. y.	ac	0	0	97	4,946,000	6.600
		Aug. 22		135½	177	89	78½	N	N	1014	c. p. y.	ac	0	0	99	4,890,000	7,120
26	X	July 5	15	122½	168½	81½	76	N	N	1013	c. p. y.	ac	Trace	0	72	4,140,000	8,450
		Aug. 22		126½	169½	82	75½	N	N	1018	c. p. y.	ac	Trace	0	98	4,640,000	4,550
27	......	July 7	15	97¼	158½	80¼	75	N	N	1020	c. p. y.	ac	0	0	87	4,898,000	4,670
		Aug. 19		106½	158¾	82	74½	N	N	1014	c. p. y.	ac	0	0	94	4,776,000	5.170
28	......	July 9	15	90	162	75¾	69	N	N	1024	c. o.	ac	0	0	67	4.320,000	7.870
		Aug. 19		103	163	79½	68½	N	N	1017	c. p. y.	ac	0	0	88	4,674,000	6,320
29	......	July 5	15	123½	169	89	77½	N	N	1015	c. p. y.	ac	0	0	96	4,896,000	8,930
		Aug. 20		127	171	90¼	77	N	N	1015	c. p. y.	ac	0	0	99	4,998,000	7,610
30	X	July 6	16	115½	163½	83	73	N	N	1003	c. p. y.	ac	0	0	86	5,020,000	9,110
		Aug. 20		116	164¼	85¼	74	N	N	1010	c. y.	ac	0	0	101	5,141,000	8 200
31	X	July 6	16	140	173	95¼	85½	N	N	1018	c. o.	ac	0	0	94	4,640,000	7,770
		Aug. 1		141	173	96½	84	N	N	1016	c. o.	ac	0	0	97	4,554,000	8.180
32	X	July 4	16	107¾	159	78½	74½	N	N	1020	c. o.	ac	X	0	100	5,122,000	6,760
		Aug. 21		114	160½	80	72	N	N	1014	c. y.	ac	0	0	97	5,001,000	7,900
33	......	July 7	16	117	165¼	84½	79	N	N	1015	c. p. y.	ac	0	0	94	4,424,000	5,680
		Aug. 21		118½	166	86½	78	N	N	1013	c. p. y.	ac	0	0	102	5,017,000	5,260
34	X	July 6	17	106	166¾	81	72½	X	N	1034	colorless	ac	0	X	87	3,998,000	8,320
	X	Died	......	......	......	......	......	......	......	......	......	......	......	......	......	......	......
35	......	July 1	17	132	167¾	90½	82	N	N	1020	c. y.	ac	0	0	97	5,080,000	9,230
		Aug. 21		140	169¼	92	83	N	N	1017	c. o.	ac	0	0	94	4.890,000	7,550
36	......	July 4	17	113	173¾	85	79	N	N	1023	c. o.	ac	Trace	0	71	4,774,000	6,310
		Aug. 20		119	174½	89	79½	N	N	1014	c. y.	ac	0	0	92	4,908,000	6,040
37	X	July 2	17	137	175	87	81¼	N	N	1019	c. p. y.	ac	0	0	110	5,142,000	4,830
		Aug. 21		138½	175½	89	78½	N	N	1019	c. p. y.	ac	0	0	97	4,983,000	6,980
38	......	July 8	17	133	169½	88	79½	N	N	1016	c. y.	ac	0	0	94	5,231,000	9,120
		Aug. 26		136½	169¾	90½	79½	N	N	1012	c. p. y.	ac	0	0	103	5,070,000	6,100
39	X	July 1	18	113¼	168½	81	75½	N	N	1018	c. o.	ac	0	0	69	4,130,000	14 000
		Aug. 18		119½	169	84½	77	N	N	1020	c. p. y.	ac	0	0	96	5,311,000	5,880
40	......	July 4	18	109½	165	83	77½	N	N	1022	c. y.	ac	0	0	83	4,273,000	8,350
		Aug. 19		117	165½	85	78½	N	N	1017	cl. y.	ac	0	0	95	4,899,000	7,640
41	......	July 4	19	112½	163	86	77½	N	N	1020	c. y.	ac	0	0	87	5,002,000	9,370
		Aug. 19		113½	164¼	87	75½	N	N	1019	c. p. y.	ac	0	0	91	4,864,000	5,730
42	......	July 2	20	160	171¾	96	87½	N	N	1015	c. p. y.	ac	0	0	82	4,373,000	6,930
		Aug. 18		158	172	97	87	N	N	1017	c. p. y.	ac	0	0	96	4,990,000	8,150
43	......	July 8	21	163	181½	87	83	N	N	1014	c. p. y.	ac	0	0	78	4,140,000	8,300
		Aug. 26		165	181¾	88	83½	N	N	1018	c. p. y.	ac	0	0	93	4,833,000	7,760

Light-faced type indicates the record at the first examination; heavy-faced type denotes results of second examination. N, negative; X, something abnormal which is discussed below; c., clear; cl., cloudy; p., pale; y., yellow; o., orange.

wholesome food, no drugs were administered for this condition. Certain of the more anaemic boys were advised to eat raw or soft-boiled eggs and to drink large quantities of milk. In fact milk figured most extensively in the menu of each meal, from sixty to seventy-five quarts being consumed a day.

The record of a few of the campers is not given since they came for too short a time. In measuring and weighing the boys, I was greatly aided by Mr. Charles W. Mayser, of the Montclair Academy, N. J., who was formerly athletic instructor at Yale, and whom I wish to thank for his assistance. The haemoglobin tests were made with the Sahli instrument. Just before the second examinations, certain of the boys had within a day or two completed a 250-mile tramp through the Adirondacks, and others had taken part in an athletic meet. Hence the weights and blood tests were probably somewhat lowered.

Discussion of Cases.

Weight and height.—These statistics are self explanatory. That the boys should have gained so markedly, when one considers the rowing, swimming, walking, racing, tennis and field athletics, is somewhat remarkable. That they gained in strength is easily believable, and I noted that their muscles were firmer and that the "student stoop" had disappeared from several who were studiously inclined. Next year it is hoped that a standard strength test will be taken of each boy.

Chest expansion and contraction.—In this list there is shown a decided development not only in the greater ability to expand, but also in the increased power to contract the chest wall. All of these measurements were made on the nipple line.

Heart and lungs.—There was only one serious heart case in camp, and this had been previously diagnosed and was under treatment. This boy (case 12) had mitral insufficiency following rheumatism, and had to be most carefully watched. He gained somewhat in weight, and to a certain extent in haemoglobin, and returned home in much better condition. Case 34 is also noted (X), but this will be taken up later. Case 6 exhibited definite signs of emphysema, and had a tuberculous history.

Urine.—All boys were advised to drink large quantities of milk and water, and to this I ascribe the lowered specific gravity and the disappearance, in all except one case (26), of the traces of albumen (1, 3, 7, 11, 16, 21). This albuminuria was, of course, the transitory albuminuria of adolescence, and no casts were found microscopically. The cloudiness in the noted cases (16, 23, 40) was due to phosphates and urates.

Sugar was found in one instance and to this I particularly wish to call attention. This boy, whose various weights and measurements are tabulated under case 34, came to camp outwardly in good health. He was not in the best of spirits nor did he take great interest in athletics or studies. This, however, his friends said had been his condition for at least a year. Upon examining the urine a most decided reaction was given with both Fehling's and Nylander's reagents. His father was straightway notified and a specimen of urine was sent to Dr. B. H. Stone, of the Burlington (Vt.) State Board of Health, for verification. Eight per cent of sugar was found. The urine was colorless, syrupy, and very sticky. The patient upon being questioned gave a history of frequent and copious micturition, great thirst, ravenous appetite, and a general feeling of depression. All of these symptoms had lasted for more than one year. His heart was rapid and irregular at times. The patient was put on a diabetic diet, but no change was noted in the percentage of sugar until July 20, when there was a lessened output of sugar but the presence of a large amount of albumen. On July 21, fifteen days after the first examination, he felt unwell. At 2 a. m., July 22, he suffered the first suppression of urine, was catheterized, carried immediately to a Burlington hospital, arrived in a comatose condition, and died at 7.30 the same evening.

What I wish to emphasize is by no means novel. Every growing boy, and for that matter every adult, should have a thorough physical examination at least once a year. The dental profession has at last persuaded the public that seasons of toothache are not the only times when the dentist is necessary, and there is no more reason why organic disturbances should be allowed to manifest themselves before the physician is notified than why a tooth should be left until its ache proves its pathological condition.

Blood examination.—Many of the boys were anaemic as before stated (cases 3, 4, 7, 10, 11, 13, 17, 21, 26, 30, 39) and a diet of eggs and milk was prescribed. A glance at the statistical record will show the marked improvement in these cases. The leucocytosis in case 34 was due to an infected foot.

Summary.—In reviewing this record one cannot fail to see the great improvement in the condition of the boys, and it is the hope of the writer that this brief article will stimulate the growth of summer camps, and their more careful supervision by the medical profession.

STUDIES IN GENITO-URINARY SURGERY

THE JOHNS HOPKINS HOSPITAL REPORTS, Volumes XIII and XIV, now ready. Volume XIII consists of about 605 pages with 201 figures in the text, six plates and one colored chart.

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NOTES ON NEW BOOKS.

Atlas of Cutaneous Morbid Histology. Consisting of fifty-three colored figures on twenty-four plates and text. By Dr. Max Joseph and J. B. Van Deventer. (*Chicago: W. T. Keener & Co., Publishers, 1906.*)

In this Atlas there are represented highly colored drawings by Dr. Van Deventer of the morbid histology of 48 skin diseases, of which 16 are rare diseases. Representations of many common diseases are left out entirely, e. g., eczema. The only drawings of syphilitic lesions are lichen syphiliticus and glossitis gummosa, the latter being a very uncommon manifestation of the disease. The common varieties of syphilis are not represented at all. Since there are so many drawings of rare diseases and none at all of many common diseases the Atlas is not very useful to students or practitioners of medicine.

To the dermatologist the Atlas will be useful, but many of the drawings are to be criticized, as they do not represent well what is actually seen in the sections. Dr. Van Deventer has not drawn what such a good authority as Max Joseph has seen in the sections. In many of the lesions the disease is of an acute, inflammatory nature, yet no polynuclear leucocytes are seen in the drawing. An example of this is seen in Plate II—Acne Urticata. The drawings are often good impressionist pictures, but the details are very poor, whereas what is wanted in miscropical drawings is especially good detail. Take one example in the Atlas, viz., the drawing representing the morbid histology of Herpes Zoster, Plate VIII, page 16; it has not the least likeness to what is actually seen in sections of this disease. Compare this drawing with the colored drawings of Kopytowski in the Archiv. für Dermat., Vol. 54, page 18, where the histological pictures are correct.

The carcinoma primarium section is drawn fairly well, but that of c. secundarium is badly represented. The drawing of the section from follicles is not very good, and there does not appear to be any cellular infiltration into the corium in the drawing of leukoplakia buccalis.

The drawings which can be said to be very good are those of angiokeratoma, erythema exudatorium multiforme, variola, glossitis gummosa, molluscum contagiosum, ichthyosis hystrix (the blood vessel in the corium ought not to be left open at each end), pityriasis rosea, lichen r. planus and verrucosa, lichen syphil. lymphangioma simplex, lupus erythemat., and vulgaris, mycosis fungoides, purpura, tubercul. cutis verrucosa, ulcus durum, verruca vulgaris, and xanthoma diabet.

The descriptions by Max Joseph, an eminent dermatologist, are given in a succinct and clear manner.

Elementary Manual of Regional Topographical Dermatology. By R. Sabouraud. Translated by C. F. Marshall. (*New York: Rebman Co., 1906.*)

When a practitioner or student is confronted with a case of skin disease, and has not had an extensive training in this branch of medicine, he finds great difficulty, even with a good text-book beside him, in diagnosing the case because he does not know what portion of the text-book to consult. Sabouraud's work attempts to obviate this difficulty.

The classification of skin diseases in the large majority of text-books on dermatology is based on a pathological plan which was originally Hebra's idea. A few text-books have been written where the diseases have been arranged alphabetically. Sabouraud's idea is an original one as far as text-books are concerned, but the plan has been in practical use in the Johns Hopkins Medical School for the last eight years, where there have been supplied to the students typewritten notes, wherein the common skin diseases have been arranged regionally and also according to their primary lesion.

In Sabouraud's text-book, which consists of 660 pages and is fairly well illustrated, the various regions of the skin are taken in order, beginning with the face, and a list of common and rare diseases is given first, then a description follows of each affection. The rare diseases are mixed with the common, which the writer thinks is a mistake.

The description of the common diseases is very incomplete and much too short. This plan of division involves a great deal of repetition of the same disease in many chapters scattered throughout the book. It would have been better and more practical to simply give a list only of the diseases in the different areas and then later consider the diseases fully and properly. The treatment is usually limited to a few remedies for each disease and the modern methods are mentioned as far as X-rays, and high frequency currents are concerned, but there is no reference to opsonic treatment.

No pathology is given and the etiology is often dismissed in a few words and is sometimes not very reliable. Yet with all these faults the text-book is a good one; it shows individuality, and although the descriptions of the diseases are short, they are to the point and are practical. It is valuable if only for the lists of skin diseases which attack the different regions of the body. The illustrations are fair when one compares them with the excellent reproductions in some of the larger American text-books.

Schleif's Materia Medica and Therapeutics. A Pocket Text-Book of Materia Medica, Therapeutics, Prescription Writing, Medical Latin and Medical Pharmacy. By William Schleif, Ph. G., M.D., University of Pennsylvania, Philadelphia. New (3d) edition, 12mo. 470 pages. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

The present volume presents the subjects of materia medica and therapeutics in the usual way and appears to be quite complete in the number of remedies discussed. Many of the newer synthetic compounds are included.

As is necessary in a "pocket-book," the treatment of the subject matter is very concise. In fact, we believe that the paragraphs, particularly those devoted to the physiological action of the various drugs, are much too brief—so brief, indeed, as to interfere with the author's statement in the preface that the book "contains . . . the essential knowledge required in the most complete college courses on Materia Medica and Therapeutics." For those preparing for State board examinations, for example, who wish quickly to review the main facts in regard to the various drugs, the volume is admirable, but for undergraduates it seems unsuitable as a text-book. The teaching is too dogmatic and the discussions, as a rule, too abbreviated.

The Essentials of Histology, Descriptive and Practical. For the use of Students. By C. A. Schäfer, LL. D., Sc. D., F. R. S., etc. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

The seventh edition of Schäfer's Essentials of Histology presents a neat appearance, is strongly bound, and is printed upon good paper in clear type.

The subject matter is divided into fifty chapters or "lessons," for conveniently accompanying the work of a class. As a preface to each lesson, are given practical directions for the preparation and study of the tissues described in the text of the ensuing lesson. The text presents in clear descriptions the essentials of histology, omitting less important details. The illustrations are profuse and

accurate, being selected largely from other authors. The coloring of some of the illustrations is a new feature of this edition. The colored illustrations often give the student a better idea of what he should see in the stained section. Much has been added to the chapters on the nervous system. Many of Cajal's original drawings are reproduced in these chapters.

An appendix explains the principal methods of preserving, hardening, embedding, cutting, and staining tissues.

A Text-Book of Diseases of Women. By J. CLARENCE WEBSTER, B. A., M. D. Edin., F. R. C. P. E., F. S. S. E., etc. (*Philadelphia and London: W. B. Saunders Company, 1907.*)

The author of this text-book is to be commended for the successful treatment of a subject, which he recognizes as consisting of more than merely the pelvic organs of women. This broad treatment of the subject characterizes the book throughout, and imbues one with confidence in a specialist who teaches not only the greatest sympathy with every phase of the patient's being, but recognizes as well the minor as the major methods of the specialty. The student or general practitioner who turns to this book for advice and instruction will find comfort in the simplicity as well as directness of the handling of the subject matter contained therein.

Its practical application has lost nothing by the scientific basis upon which the book is written, and the scientific views are up to the present day, and embodied in such form as to be of practical use.

It covers the field of gynæcology, as the general practitioner is likely to see it, and treats the subject in such a way that he will be able to use it. The author is conservative without being narrow, and progressive without being extreme.

The book is well gotten up; the paper, binding, and typography are excellent, the illustrations, though not as elaborate as are found in some of the recent text-books, fulfill the purpose for which they are intended.

The Principles and Practice of Dermatology. By WILLIAM ALLEN PUSEY, A. M., M. D., etc. (*New York and London: D. Appleton & Company, 1907.*)

Revised editions of old works and new books on skin diseases brought out during the past five years have placed the text-books on dermatology at a very high plane. The latest of these is Pusey's Principles and Practice of Dermatology. This compares favorably with its predecessors and is a standard work.

Considerable attention is given to the principles of dermatology and the writer has offered many new ideas. Under general pathology some very good illustrations are used to make clear the origin of diseased conditions. The discussion of treatment in general is very good and many formulæ are given which, however, are not written in any uniform system. More thought has been bestowed on classification than the result seems to be worth; three new classes of disease being added without in any degree clearing the situation.

The amount of work done is well attested by the numerous references given under each disease. A sufficient amount of space is furnished to each disease to give a good idea of its clinical and pathological appearance, but the differential diagnosis could be made more comprehensive. Special treatment is one of the best features of the book. For a worker who has had so much experience in electro-therapeutics, it is refreshing to see with how much conservatism the author regards the value of the X-rays.

The work is fully illustrated with 356 illustrations. Quite a number of these, however, are not of much value, because they do not show sufficient detail to give one an idea of what they are intended to represent. We are glad to see only one colored plate. As a rule these are of such indifferent coloring and poor execution as to be worse than useless.

The binding of cloth is hardly strong enough to support the weight of the book, but the paper and printing are both good.

Deutsches Bäderbuch. Quarto, civ. + 536 pp. and 13 plates. (*Leipzig: Weber, 1907.*)

This important work is published under the auspices of the German Imperial Health Office and is designed to give an unbiased account of the leading German baths, mineral waters, and "Luftkurorte." Authoritative analyses of about 650 springs are given; with these is given much information concerning the climate, rainfall, etc., which will be of great value to anyone contemplating a visit to one of these springs.

There is a series of introductory chapters which make the work of very general interest to physicians, i. e., aside from any special reference to the German springs. Probably no better summaries of the present status of our knowledge concerning the pharmacology and general therapeutic uses of hot, cold, and carbon dioxide baths, and of the various kinds of mineral waters are to be found than in the chapters contributed by Jacobi (of Göttingen) and F. Kraus (of Berlin). The radioactivity of the springs is briefly discussed from both the chemical and clinical standpoint. Other introductory chapters treat of geology, climatology, and practical considerations concerning the construction of baths, etc.

This is probably the most comprehensive work ever published on the baths and springs of any country; it will be a valuable addition to medical and other libraries.

A Manual of Hygiene and Sanitation. By SENECA EGBERT, M. D., Professor of Hygiene in the Medico-Chirurgical College, Philadelphia. New (fourth) edition, thoroughly revised. 12mo., 498 pages, with 93 illustrations. (*Philadelphia and New York: Lea Brothers & Co., 1907.*)

In his preface the author says: "The Science of Hygiene has become so extensive that many volumes might be devoted to the discussion of its principles and the details of their application. Consequently the author will be content if the book continues to serve its purpose as a simple 'manual.'" With this limitation in view Dr. Egbert has succeeded in writing an excellent manual, well balanced, well arranged, and up-to-date. It is an entirely satisfactory work for a student's first course in hygiene. Most persons fail to appreciate the full meaning of the word hygiene, which, as Parks says, "signifies rules for the perfect culture of mind and body," and this makes clear why it is impossible to treat the entire subject in a single volume. Hygiene and sanitation are almost synonymous terms and to show the difficulty of treating this branch of medicine in small compass I again quote from the author, p. 282: "The essence of sanitation is to secure perfect health, to increase the inherent power, to resist noxious and harmful influences, and to make all the surroundings and environments of the body pure and free from depressing factors." Dr. Egbert has divided his work into 15 chapters as follows: Introduction, bacteriology, the atmosphere-air, ventilation and heating, water, food, stimulants and beverages, personal hygiene, school hygiene, disinfection, quarantine, the removal and disposal of sewage, military hygiene, vital statistics, and the examination of air, water, and food. Each chapter is concise and clear, and the work is written so as to be interesting. A few misprints have been noticed, clearly due to the enlarging of the text, and the failure to make the references on a given page agree with the new paging (ex. p. 170, 8 lines from bottom for 213 read 220; p. 176, 2d paragraph 6th line for 165 read 169; there are similar errors on pp. 271 and 308). R. N.

Immune Sera. By DR. CHARLES FREDERICK BOLDUAN. Second edition, rewritten. (*New York: John Wiley & Sons.*)

This work is a revision of the author's translation of Wassermann's monograph published in 1904, and in addition to the excel-

lent material of the first edition contains new chapters on snake venoms, agglutinins, opsonins, and serum sickness. In the discussion of opsonins the author takes the conservative stand held by most American investigators, and in the chapter on serum sickness he gives a report of Gay and Southard's recent studies on Anaphylaxis. The new portion of the book reaches the same high standard as the original. The material is well chosen, the style is simple—a matter of no little importance in such a condensed work—and on the whole the book is an excellent exposition of the most essential facts and theories bearing on the field of immunity.

The Diseases of the Eye. By G. E. de Schweinitz, A. M., M. D. 5th edition revised. (*Philadelphia and London: W. B. Saunders Company, 1906.*)

This splendid work is a revision of four former editions with so much more added as to bring it abreast with modern medicine.

The work is divided into twelve chapters, each chapter taking up and considering in a concise but not too brief manner a single subject. These subjects are first considered in a general way so as to develop the subdivisions, then the subdivisions are taken up and minutely discussed. No single chapter can be selected as the best, they are all the product of a finished authorship and the work of an exceptional ophthalmologist.

In revising the older editions the author has re-written many of the chapters so as to make them conform to modern ideas; he has also added many paragraphs on subjects not considered in the older works.

The most delightful part of the book is that no space is wasted on unproved theories. Where a subject is still under dispute both sides of the controversy are succinctly given; where the weight of the author's experience forces him to lean in one direction he frankly states his views without dragging in a long line of useless argument.

The index, occupying, as it does, fifty pages, is one of the most valuable parts. It is possible to find any subject or subdivision of any subject without trouble.

This work is certainly one of the best text-books on ophthalmology extant and probably the best by an American author.

Röntgen Rays and Electro-Therapeutics. By M. K. Kassabian, M. D. (*Philadelphia and London: J. B. Lippincott & Co., 1907.*)

As the title indicates, the author has endeavored to cover the field of electricity and its allied branches as applied to medicine. The first section of the book is devoted to electro-therapeutics and in it the author describes the various forms of medical electrical apparatus and methods of application.

The second section is devoted to Röntgen Rays. This section is a more important one. The author has devoted 450 of the 550 pages of the book to this subject which is well handled and attractively presented.

The chapters on apparatus and dosage deserve more than passing notice. The various forms of X-ray apparatus are not only described, but the principles are explained so that one gets an intelligent understanding of the actual working of the various parts. The chapter on X-ray dosage is especially valuable.

Unfortunately so far no one has been able to elaborate a standard unit of dosage and consequently there are many methods of treatment in vogue. The author has taken great pains to collect and summarize these various methods. Thus we are able to get in a glance what would otherwise cause the reader to search through many books and monographs. The numerous and excellent illustrations add greatly to the value of the book.

Elements of Human Physiology. By Ernest H. Starling, M. D. London, F. R. C. P., F. R. S. Eighth edition. (*Chicago: W. T. Keener & Co., 1907.*)

According to the preface, the author's aim in this work is "to present in the shortest possible compass the essentials of the Science of Physiology." This, the eighth edition of this text-book, is considerably larger than any of the previous editions and comprises slightly over seven hundred pages. The first chapter is an "Introduction" of twenty-four pages and is concerned with a short account of physiological processes, such as assimilation, respiration, circulation, co-ordination, reaction, and reproduction, viewed in a general biological sense. Following this is a chapter upon the chemistry of the body, and then the more special physiological processes are treated in the usual order and grouping.

The book as a whole is excellent, and is written in the clear concise style of the author. The terseness of expression is in many places very attractive, as for example in the first paragraph of the chapter upon Lymph and Tissue Fluids (p. 286): "The blood flows in capillaries with definite walls consisting of a single layer of cells, and is thus separated from the tissue elements. . . . A middleman is thus needed between the blood and the tissues, and this middleman is the lymph . . . ." In other instances it is with the sacrifice of absolute accuracy, as for example in the chapter on the Ductless Glands, "Under this title have been grouped a number of organs, the sole resemblance between which lies in the fact that we know very little about them" (p. 513).

In a work of this scope, which treats of such a broad subject as physiology, it is extremely difficult to present the salient features of a subject and avoid a lengthy presentation of different views. A certain amount of positiveness of statement no doubt is useful to avoid confusing the elementary student. Nevertheless, the main adverse criticism that can be applied to this text-book is in certain subjects a tendency to regard undecided questions as settled and to leave the student with one idea concerning them. In one instance at least the conclusion is rather surprising. "It seems therefore highly probable that the normal reflex or voluntary contraction is not a tetanus (a condition which is a product of the physiological laboratory), but a prolonged single contraction caused by a constant stimulus arriving at the muscle from the central nervous system" (p. 148). The author sheds no new light upon this old question. He gives the sequence of contraction in the mammalian heart to be respectively great veins, auricles, ventricles (p. 210), and states that the contraction of the muscular rings at the mouths of the great veins always precedes the auricular systole and prevents regurgitation of the blood into the veins when the auricle contracts (p. 211). He regards the neurogenic theory of the heart-beat as a dead issue (p. 237). He states that reflection from the periphery cannot explain the production of the dicrotic waves (p. 230), and gives the old objection, that no matter from what portion of the arterial tree the tracing is made, the dicrotic notch always occupies the same place on the pulse wave. This disposes of a theory which has not been seriously entertained for a long time, but it leaves out entirely the very important view held by v. Kries and others, that the dicrotic wave is due to a double reflection.

In view of the present importance of the venous pulse and its constantly increasing occurrence in medical literature, it is rather surprising that no reference is made to it.

No references to the literature are given. Individual authors are, however, frequently referred to by name. Even in a work of this scope it would seem useful to the student, for the purpose of collateral reading, to have a few references to carefully selected articles of fundamental importance.

This edition of Prof. Starling's work places before the medical student a text-book well fitted for his needs. The situation in regard to carefully written, concise, and yet somewhat comprehensive physiological text-books for English reading medical

students has been greatly improved in the last few years by the publication of one or two excellent works, to which this book, in its present form, is a worthy addition. Remarkably good chapters are those upon Digestion and Secretion, and Metabolism. The latter especially is a clear, concise presentation of the salient features in a remarkably brief compass, and fulfills well the desire of the author as expressed in the preface.

J. A. E. EYSTER.

The Diseases of the Digestive System. Edited by FRANK BILLINGS, M. D. Authorized translation under supervision of JULIUS L. SALINGER, M. D. (*New York and London: D. Appleton & Company, 1906.*)

This is a collection of monographs by German authors which appeared as Vol. V of Die Deutsche Klinik. As these articles originally appeared during the years 1901-5, the material cannot be said to be absolutely new and is familiar to those who have followed the publications appearing as Die Deutsche Klinik. Each individual writer treats of the subject with which he is most familiar and in which, as a rule, he has done pioneer work. The book, therefore, gives one an insight into the very best work which has been done in diseases of the digestive system. Such a plan of having text-books written by several authors seems to be a necessary result of the present high grade of specialization in medicine, and so long as the writers are the leading exponents of the subjects on which they write, as in this case, no objection can be raised to the method, and much may be said in favor of it. In the present instance the list of writers includes such men as Rosenheim, Riegel, Ewald, Boas, Oser, Minkowski, Vierordt.

Not only are diseases of the stomach and intestines thoroughly treated, but a splendid article on diseases of the pancreas by Oser is included, and diseases of the liver and gall stones are exhaustively considered. Probably the least satisfactory section of the book, from the standpoint of the American physician and surgeon, is the one on acute diffuse peritonitis, appendicitis, and perityphlitis. One notes with interest what a straining there is to give rules for the differential diagnosis of the various forms of appendicular inflammation. It is admitted, however, that "*exceptions to all these rules occur and in all directions.*" The writer begs the question as to operative procedure, and finally concludes that in the individual case one must be largely influenced by the skill of the attending surgeon and the confidence one has in his ability.

An interesting chapter is contributed by Strasburger on the examination of the feces.

The translation has been well done, the typographical work is excellent and altogether it is a most attractive book. The editor has contented himself with seeing that the views of the writers are faithfully reproduced and has not added to or modified the text to any important extent. Very few references are given, some are omitted which were given in the original publication. It does not pretend to be a reference book, however, but a work for the guidance of those treating disease, and for that reason is a most valuable book for the general practitioner.

Practice of Obstetrics by American Authors. Edited by CHARLES JEWETT, M. D., Professor of Obstetrics and Gynecology in the Long Island College Hospital, New York. Third edition. Revised and enlarged. (*New York and Philadelphia: Lea Brothers & Co., 1907.*)

The list of contributors to this volume includes, among others, such well known teachers as Dickinson, Edgar, Henrotin, Jewett, Robb, Webster, and Williams. This selection of itself is strongly commendatory of the book and would give it an unusual value were it not that these men either have their own individual text-books, or have contributed largely to other treatises on obstetrics. Therefore, in many parts the present work is practically a reprint of sections in contemporary text-books.

The illustrations are almost entirely adopted from other publications. Bumm's excellent drawings have been freely used and likewise the admirable diagrams of Faraboeuf and Varnier. For these credit is frankly given.

That part of the book which deals with obstetrical anatomy and pathology is notably deficient in microscopical considerations, both with regard to text and illustration. Those pictures which have been inserted are sometimes inaccurate; thus in one of the colored plates (XIV) several of the chorionic villi are designated blood sinuses. Too scant attention is given to the implantation of the ovum, the formation of the membranes, and the development of the placenta. While, on the other hand, more space is allotted to embryology than would seem necessary to the study or practice of Obstetrics.

The clinical side of parturition and the care of the mother and child in the post partum period are adequately and clearly treated. It is to be regretted that advice is still given to apply an abdominal binder immediately after the completion of labor. Experience has shown that its use is not of any benefit to the patient and may do considerable harm, since backward displacements of the uterus are more commonly observed in cases where the binder has been used.

Autointoxication during pregnancy is dealt with in a confused manner. All manifestations of such a state are considered to be dependent upon the same organic changes, and designated, "The Toxæmias of Pregnancy." This is surprising, since Stone, who writes this section, was one of the first to call attention to the liver changes in pernicious vomiting and their similarity to acute yellow atrophy, which is quite different from the liver condition of eclampsia.

The chapters on obstetric surgery catalogue very completely the various operations which aim at delivery. It is not in accord with present opinion, however, to concede eleven pages to symphysiotomy and merely give passing mention to pubiotomy. The latter has proven itself a valuable addition to operative obstetrics supplying the advantages gained by cutting through the symphysis, without the immediate and remote complications which frequently attend this procedure.

The Quarterly Journal of Medicine. Edited by WILLIAM OSLER, J. ROSE BRADFORD, A. E. GAUNOD, R. HUTCHISON, H. D. ROLLESTON, and W. HALE WHITE, with the help of T. CLIFFORD ALLBUTT, BYRON BRAMWELL, and others. Vol. I. Number 1. (*Oxford: At the Clarendon Press. London, New York,* and *Toronto: Henry Frowde, October, 1907.*)

This new English journal is the official organ of the lately formed Association of Physicians of Great Britain and Ireland. It "will be devoted to the publication of original papers dealing with Clinical Medicine . . . It will include critical reviews on special subjects and diseases, but with this exception the journal will be entirely concerned with original communications." Such are the objects of the journal as stated in the advertising sheet. The multiplication of medical journals is not to be generally advocated—there are already far too many, but there would seem to be a place for such a journal as this, especially in England, where no quarterly covering the same ground already exists. This number contains 13 papers, all well worth reading. The journal is abundantly and well illustrated, some of the reproductions being in color. If the editors are able to publish each quarter a number with articles of as much interest as those presented, the journal cannot fail to be a success and will be welcomed not only by the profession in England but in Europe and America as well. It is to be hoped that it will meet with the support it deserves, for the present number could hardly be improved upon in the quality and variety of its contributions.

The journal is of a pleasing size and type, altogether dignified and worthy of the Clarendon Press.

R. N.

Progressive Medicine, Vol. III, September, 1907. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M. D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia. Octavo, 290 pages, with 15 engravings. (*Philadelphia and New York: Lea Brother & Co., Publishers.*)

In this volume the diseases of the thorax and its viscera, including the heart, lungs, and blood-vessels, have been discussed by Dr. W. Ewart; dermatology and syphilis by Dr. W. S. Gottheil; obstetrics by Dr. E. P. Davis, and diseases of the nervous system by Dr. W. G. Spiller. Each of these contributors is a recognized leader in his own specialty, so that their remarks on the progress made in these branches of medicine are well worth reading and serious thought. By securing the services of such men, the editors of this series have been able to issue quarterly volumes of distinct value to the general practitioner who has not the means or the time to keep up with the most important contributions to medicine, which appear all over the world in a variety of languages. For this reason "Progressive Medicine" can be recommended to the medical profession at large as a most serviceable handbook. Each volume contains a few illustrations, and is furnished with a good index. R. N.

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